The Presence and Predictive Capacity of Altered Cervical Kinematics, Neuromuscular, and Psychological Features in Individuals with Whiplash Associated Disorders at Different Stages of Pain

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Abstract

Neck pain is a significant source of disability and is associated with reduced quality of life and reduced work productivity. Besides the burden of current neck pain, neck pain disorders are commonly recurring conditions, with episodes of pain reoccurring over the course of months or years. Individuals with Whiplash Associated Disorders (WAD) are more likely to present with higher pain severity and greater physical and psychological impairments than individuals with idiopathic neck pain.

This thesis presents an investigation of features related to cervical kinematic, neuromuscular, and psychological function in individuals with acute, recurrent, and chronic neck pain (CNP) following a whiplash trauma, and assesses their relevance for the presence of persistent pain and disability. Four studies were conducted to investigate this aim.

Study 1 assessed cervical kinematic features in people with acute WAD and assessed their correlations with self-reported outcomes. Compared to healthy participants, cervical range of motion, velocity of movement, and smoothness of movement were altered in people with acute WAD and the extent of these features were associated with the level of neck pain and disability.

Study 2 comprised a systematic review to assess whether the cervical kinematic features identified in Study 1 were predictive of ongoing pain and disability after a whiplash trauma. Low to very low-quality evidence indicates that high levels of pain and disability at baseline as well as a higher WAD grade were associated with poor outcomes. Inconclusive evidence was found on the predictive capacity of neck range of motion, joint position error, activity of the superficial neck muscles, muscle strength/endurance, and perceived functional capacity. No primary studies investigated the association between more contemporary kinematic features such as velocity of neck movement, smoothness of movement, and

variability of neck motion with ongoing disability following a whiplash injury. Findings from this review prompted the need for Study 3.

The initial aim of Study 3 was to investigate the predictive ability of cervical kinematic features on pain and disability six months following a whiplash injury. However, this aim was modified due to the small sample of recruited participants as a consequence of the COVID-19 pandemic. The modified aim was to assess the correlation between baseline measures of cervical kinematics and ongoing pain and disability six months later, instead of assessing the predictive ability of such features. Preliminary findings suggest that cervical kinematics in extension were correlated with ongoing pain and disability six months following the injury.

The final study, Study 4, of the thesis investigated similar features that were assessed in the other studies within this thesis, but in individuals with recurrent neck pain (RNP), or CNP following a whiplash injury, and healthy participants. All three groups had been assessed at baseline, with only the RNP group had been followed for up to a 12-months. The existence of altered cervical kinematic features, neuromuscular, and psychological function in individuals with RNP compared to CNP and healthy participants was assessed (cross-sectional design), with their predictive ability investigated in those with RNP (longitudinal design). The results indicated that people with RNP and CNP presented with higher neck disability, greater kinesiophobia, lower quality of life, slower and irregular neck movements, and less neck strength compared to healthy controls. Moreover, a higher number of previous pain episodes within the last 12 months along with lower neck flexion strength were predictive of higher neck disability at a six-month follow-up in those with RNP. These findings have significant implications for rehabilitation and prevention of patients with WAD; this work has identified features which could be targeted in a rehabilitation programme with the aim of preventing recurrent episodes of neck pain.

Overall, this thesis found that altered cervical kinematics together with impaired psychological function are present soon after a whiplash injury and can remain present in people with CNP, and in people with RNP even when assessed during a pain-free period. Furthermore, preliminary findings highlighted the association between altered cervical extension with ongoing pain and disability following a whiplash trauma, and that the number of previous episodes of neck pain over a 12-month period together with lower neck muscle strength were predictive of higher neck disability at a six-month follow up in people with RNP. Greater understanding of the physical and psychological manifestations at different stages of pain and their relevance to ongoing poor outcomes has potential to influence rehabilitation programmes to ensure better patient recovery.

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List of Papers and Conference Abstracts

During my PhD, the following papers, all of which directly related to this thesis, have either been published, presented at conferences, or were in preparation at the time of thesis submission. When required, a summary with further details about the papers and how they were used in this thesis will be given at the beginning of each Chapter. Therefore, sections of this thesis are written verbatim from published work. The sections of the thesis that have been developed from published work will resemble the published work in terms of structure and content.

Published Articles

1. **Alalawi, A.**, Gallina, A., Sterling, M. and Falla, D., 2019. Are physical factors associated with poor prognosis following a whiplash trauma?: a protocol for a systematic review and data synthesis. *BMJ open*, *9*(11), p.e033298. **(Appendix 1)**

2. **Alalawi, A.**, Luque-Suarez, A., Fernandez-Sanchez, M., Gallina, A., Evans, D. and Falla, D., 2020. Do measures of physical function enhance the prediction of persistent pain and disability following a whiplash injury? Protocol for a prospective observational study in Spain. *BMJ open*, *10*(10), p.e035736. **(Appendix 2)**

3. **Alalawi, A.**, Devecchi, V., Gallina, A., Luque-Suarez, A. and Falla, D., 2022a. Assessment of neuromuscular and psychological function in people with recurrent neck pain during a period of remission: Cross-sectional and longitudinal analyses. *Journal of Clinical Medicine*, *11*(7), p.2042. **(Appendix 3)**

4. Alalawi, A., Luque-Suarez, A., Fernandez-Sanchez, M., Tejada-Villalba, R., Navarro-Martin, R., Devecchi, V., Gallina, A. and Falla, D., 2022c. Perceived pain and

disability but not fear of movement are associated with altered cervical kinematics in people with acute neck pain following a whiplash injury. *Musculoskeletal Science and Practice*, *62*, p.102633. (**Appendix 4**)

5. **Alalawi, A**., Mazaheri, M., Gallina, A., Luque-Suarez, A., Sterling, M. and Falla, D., 2022d. Are Measures of Physical Function of the Neck Region Associated With Poor Prognosis Following a Whiplash Trauma?: A Systematic Review. *The Clinical journal of pain*, *38*(3), pp.208-221. **(Appendix 5)**

Article in Preparation

1. **Alalawi, A.**, Fernandez-Sanchez, M., Devecchi, V., Gallina, A., Luque-Suarez, A. and Falla, D., 2022. Cervical kinematic features and catastrophising are associated with poor recovery following a whiplash injury: preliminary findings from a longitudinal study. **(In Preparation).**

Conference Presentations

Poster presentations

1. **Alalawi, A.**, Fernandez-Sanchez, M., Devecchi, V., Gallina, A., Luque-Suarez, A. and Falla, D., 2021. People with acute neck pain following a whiplash trauma, present with reduced range, velocity and smoothness of neck movement. Physiotherapy UK 2020 Conference, Virtual.

2. **Alalawi, A.**, Mazhari, M., Gallina, A., Sterling, M. and Falla, D., 2021. Are physical factors associated with poor prognosis following a whiplash trauma?: A systematic review. Physiotherapy UK 2020 Conference, Virtual.

3. **Alalawi, A.**, Devecchi, V., Gallina, A., Luque-Suarez, A. and Falla, D., 2021. Assessment of Neuromuscular and Psychological Features in People with Recurrent Neck Pain During a Period of Remission. IASP 21 Virtual World Congress on Pain. Virtual

Table of Contents

List of Figures

List of Tables

Abbreviations

ANOVA	Analysis of Variance
CCF	Cranio-Cervical Flexion test
CCF MVC	Maximum Cranio-Cervical Flexion Strength
CNP	Chronic Neck Pain
DRI	Disability Rating Index
EMG	Electromyography
EQ-5D	European Quality of life – Five Dimensions
GRADE	Grading of Recommendations, Assessment, Development and Evaluations
JPE	Joint Position Error
LASSO	Least Absolute Shrinkage and Selection Operator
MCU	Multi-Cervical Unit
MVC	Maximum Voluntary Contraction
NDI	Neck Disability Index
NPOS	Neck Pain Outcome Score
NRS	Numeric Rating Scale
NRS-ROM	Numeric Rating Scale after all neck movements testing
NVP	Number of velocity peaks
PCS	Pain Catastrophising Scale
PDI	Pain Disability Index
PRISMA	Preferred Reporting Items for Systematic reviews and Meta-Analyses
PROSPERO	International Prospective Register of Systematic Reviews
QTF	Quebec Task Force
QUIPS	The Quality In Prognostic Studies
REDCap	Research Electronic Data Capture
RMSE	Mean Squared Error
RNP	Recurrent Neck Pain
ROM	Range of Motion
SC	Splenius Capitis
SCM	Sternocleidomastoid
SF-36	36-Item Short Form Survey
STROBE	Strengthening the Reporting of Observational Studies in Epidemiology statement
TSK	Tampa Scale of Kinesiophobia
VAS	Visual Analogue Score
Vmean	Mean velocity
Vpeak	Peak velocity
WAD	Whiplash Associated Disorders

CHAPTER 1

GENERAL INTRODUCTION

1.1 Neck pain disorders

Neck pain is one of the most common musculoskeletal disorders worldwide, ranking first in the majority of 195 nations surveyed (Vos et al., 2017). It is the fourth most common cause of years lived with a disability, according to the Global Burden of Disease study (Vos et al., 2012), regardless of age, gender or culture (Vos et al., 2016). Furthermore, neck pain is becoming increasingly prevalent, with a 21% increase in the overall incidence of pain lasting more than three months between 2006 and 2016 (Vos et al., 2017). It is a significant source of disability and reduced quality of life (Hoy et al., 2014), activity limitations (Carroll et al., 2008a) and reduced work productivity (Boström et al., 2008), with significant social and psychological impacts (Hogg-Johnson et al., 2009).

1.1.1 **Neck pain is a recurrent disorder**

Recurrent pain is defined as two or more pain episodes (lasting 24 hours or more) with a pain intensity of at least 2/10 on the Numeric Rating Scale (NRS) separated by a period of complete remission lasting at least 30 days (Stanton et al., 2011). Besides the burden of actual neck pain, neck pain disorders are recurring conditions, with episodes of pain commonly reoccurring over the course of months or years (Haldeman et al., 2010, Hush et al., 2011). The majority of individuals who suffer from neck pain do not completely recover, and 50% to 85% of those experience it again 1 to 5 years later or develop persistent neck pain (Skillgate et al., 2012). This adds to the significant burden of neck pain disorders, which leads to more years with disability (Vos et al., 2016).

1.1.2 Definitions and classifications of neck pain disorders

Neck pain can be defined or classified based on symptom duration or mechanism of onset. Neck pain disorders can be categorised based on the duration of symptoms into acute, subacute or chronic. Acute pain is defined as pain that lasts less than three months or pain that lasts 1 day to 12 weeks (Bussières et al., 2018). Subacute pain, which overlaps with the definition of 'acute' pain, refers to pain duration that exists for 6–12 weeks (Marin et al., 2017). Chronic pain is defined as pain that lasts for more than three months (Bussières et al., 2018). Chronic pain is different from recurrent pain in that the former is continuous, with varying pain intensity and no remission (Kongsted et al., 2016). The latter has a period of complete remission of pain that lasts at least 30 days.

Besides the duration of symptoms, neck pain disorder classifications based on the mechanism of onset have been used frequently in the literature, for instance mechanical (e.g. idiopathic or non-specific) neck pain, traumatic neck pain and degenerative disorders (Jull et al., 2018). The personal and social costs of mechanical neck pain are growing, which is largely due to contemporary lifestyle, occupational factors and an increasingly ageing population (Farioli et al., 2014). Traumatic neck pain can happen during sports injuries, falls, blunt trauma or motor vehicle accidents. Whiplash-associated disorders (WAD) are commonly encountered following motor vehicle collisions (Pastakia and Kumar, 2011).

Individuals with WAD are more likely to present with greater impairments than individuals with mechanical neck pain (Stenneberg et al., 2021). Using comparative population averages, individuals with WAD had more pain and disability than did patients with mechanical neck pain (Anstey et al., 2016). Moreover, central nervous system sensitisation (Van Oosterwijck et al., 2013), greater physical impairments (Ris et al., 2017), changes in cervical muscle morphology (Smith et al., 2020) and impaired somatosensory function (Mazaheri et al., 2021) were more frequently exhibited in individuals with WAD than in those with mechanical neck pain. Finally, psychological features and emotional distress related to the accident were often seen following WAD (Campbell et al., 2018).

1.2 Whiplash-associated disorders

Whiplash injury is a cause of disability (Carroll et al., 2014) and frequently has negative effects, such as a decreased ability to work, fatigue, being unable to participate in certain activities, depression, frustration and anger (Pinfold et al., 2004). The term 'whiplash' refers to an injury mechanism caused by an abrupt forward and backward movement of the head (Spitzer et al., 1995). Individuals who have whiplash injury may experience a variety of clinical symptoms that are collectively known as WAD (Spitzer et al., 1995). With 83% of those engaged in car accidents suffering from WAD, it is one of the most frequent injuries related to automotive accidents (Yadla et al., 2008). Globally, the number of patients who present to hospitals with traffic-related WAD has increased over the past 30 years (Siegmund et al., 2009).

The incidence of WAD has increased, affecting an estimated 300 per 100,000 people in the Western world (Holm et al., 2009). It has major financial, psychological and emotional effects on those who have WAD, as well as their families, caregivers and the medical and legal systems (Elliott et al., 2009). For example, WAD poses a substantial socioeconomic burden (Holm et al., 2009), with annual costs of about £3 billion to the UK economy alone (Melody, 2003). This burden is mainly attributed to people who experience chronic, long-lasting symptoms of WAD, and half of those with WAD continue to experience neck pain at least a year after their injury (Carroll et al., 2008b).

1.2.1 The Mechanism of Injury

The understanding of how whiplash injuries occur has changed over time. Initially, it was believed that the injury resulted from a sudden and excessive extension of the neck, leading to large angular displacements (Albert, 2017). However, more recent research suggests that the injury is caused by the body's reaction to rapid acceleration and deceleration, which leads to displacement of the head and neck without direct impact (Albert, 2017). Previously, Elliott et al. (2009) summarised the pathomechanics of whiplash injury. During a rear-end collision, the force of the car's seat propels the person's torso forward, creating an S-shaped curve in the neck and forcing it into an abnormal, non-natural movement. This movement stores energy in the neck's elastic components, which is then released suddenly, causing the head and neck to thrust forward.

Extensive research has been conducted to study the biomechanics of the cervical spine during a whiplash injury. Researchers have used various methods such as observing cadavers, testing human volunteers, and employing finite analysis modelling to gain insights (Kaneoka et al., 1999, Panjabi et al., 2004b, Pearson et al., 2004, Grauer et al., 1997). The studies consistently reveal that during the early stage (0 to 75 milliseconds [ms]) of a rear-end car collision, the cervical spine experiences an initial S-shaped phase (Pearson et al., 2004, Panjabi et al., 2004b, Kaneoka et al., 1999). In this initial phase, the car seatback propels the torso forward (0-50 ms after impact), causing the thoracic and cervical spine to straighten (Bogduk and Yoganandan, 2001). Subsequently, between 50 and 75 ms, the car seat rapidly thrusts the occupant's torso forward, while the head remains stationary due to inertia (Figure 1.1).

1998).

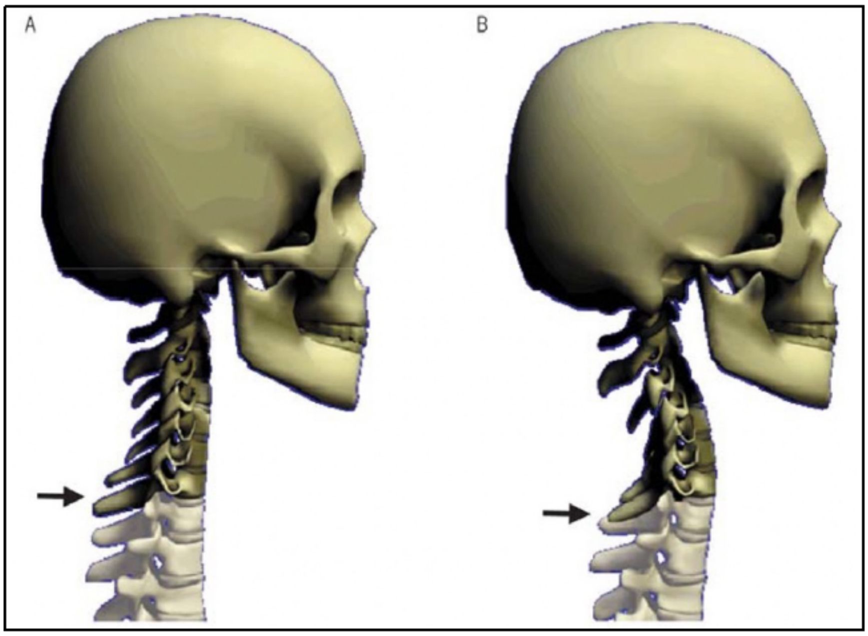

Figure 1.1: (A) Critical period from where the spine goes from a straightened position (0-50 milliseconds) to the abnormal 'S-shaped' curve (50-75 milliseconds). (B) It is here (50-75 milliseconds) that the facet capsules can be stretched, pinched, and torn. Reproduced with permission from (Elliott, J.M., Noteboom, J.T., Flynn, T.W. and Sterling, M., 2009. Characterization of acute and chronic whiplash-associated disorders. journal of orthopaedic & sports physical therapy, 39(5), pp.312-323 [https://www.jospt.org/doi/10.2519/jospt.2009.2826]). Copyright ©Journal of Orthopaedic & Sports Physical Therapy®, Inc. Permission is available in Appendix 6.

At around 100-120 ms, the occupant's torso is rapidly pushed forward from the lower cervical spine. This leads to an extension of the head and lower cervical spine as the head lowers due to the centre of gravity (Panjabi et al., 1998) (Figure 1.2). By 160 ms, the car seat has fully accelerated the torso, causing the lower neck to be pulled forward (Panjabi et al., 1998). Between 200-300 ms, the head and torso are accelerated forward of the car seat, resulting in spine flexion (Bogduk and Yoganandan, 2001). Finally, at around 600 ms, the occupant returns to their initial position (Bogduk and Yoganandan, 2001, Panjabi et al., 1998).

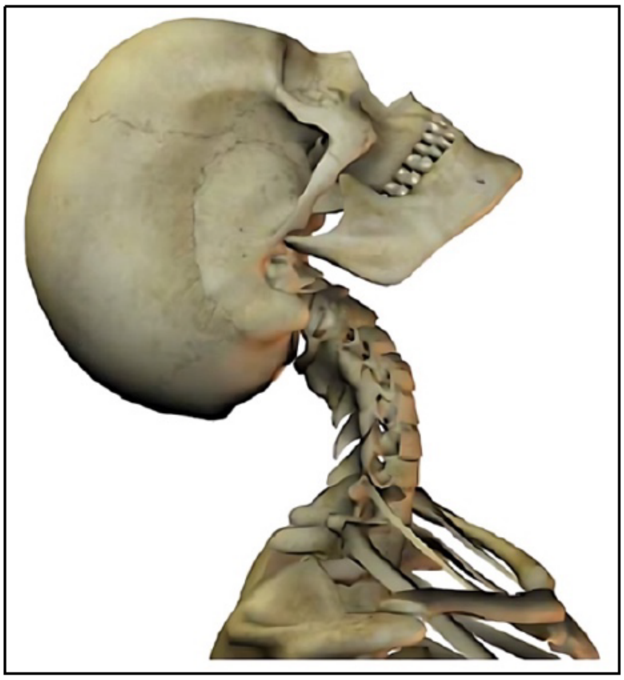

Figure 1.2: Illustration of the second phase of the 'S-shaped curve' (>100 milliseconds); the torso has pulled so far forward on the lower neck that the head is forced backwards over the head restraint. Depending on the severity of the collision, the ligaments in the anterior portion of the spine can be injured during this phase of the collision. Reproduced with permission from (Elliott, J.M., Noteboom, J.T., Flynn, T.W. and Sterling, M., 2009. Characterization of acute and chronic whiplash-associated disorders. journal of orthopaedic & sports physical therapy, 39(5), pp.312-323 [https://www.jospt.org/doi/10.2519/jospt.2009.2826]). Copyright ©Journal of Orthopaedic & Sports Physical Therapy®, Inc. Permission is available in Appendix 6.

A significant portion of this involuntary motion occurs with minimal or no resistance from the paraspinal muscles that provide support. This is because it takes significantly longer to trigger reflexive muscular activity, and as a result, there is little to no resistance from the supporting paraspinal musculature during these motions (Panjabi et al., 1998).

1.2.2 Pathoanatomical Lesions in WAD

The whiplash injury can cause damage to various structures of the cervical spine (Elliott et al., 2009). This is supported by evidence from bioengineering studies that have identified the possibility of lesions occurring, as well as cadaveric studies where lesions have been demonstrated in non-survivors of motor vehicle collisions (Yoganandan et al., 2002, Taylor and Taylor, 2014). Structures that may be damaged include intervertebral discs, ligaments, facet joints, muscles, and nerve tissues (Hubbard et al., 2008, Tominaga et al., 2006a, Stemper et al., 2006, Panjabi et al., 2006, Ivancic et al., 2006, Rothman et al., 2005, Panjabi et al., 2004a, Ide et al., 2001). However, providing an exhaustive account of all the soft tissues damaged in individuals with WAD is beyond the scope of this thesis. Therefore, this thesis will focus on the findings related to damage in the facet joints, neck ligaments, and neck muscles only.

1.2.2.1 ***Muscle injury***

Studies have indicated that the sternocleidomastoid (SCM) muscle is susceptible to injury during a whiplash incident (Brault et al., 2000). In particular, one study found that this muscle contracts rapidly during a simulated rear-end impact, which can result in muscle injury due to lengthening (eccentric) contractions (Brault et al., 2000). Additionally, recent evidence has indicated that the semispinalis, splenius capitis (SC), and upper trapezius muscles in the posterior region of the neck experience larger strains after a whiplash injury, compared to the SCM muscle (Vasavada et al., 2007). These larger strains in the neck extensor muscles align with patient reports of experiencing pain in the back of their neck following a rear-end collision.

1.2.2.2 ***Ligaments***

According to Tominaga et al. (2006b), a simulated rear-end vector impact during a whiplash injury may cause microscopic sub-failure injuries to cervical ligaments in the mid- and lower-cervical segments, resulting in reduced strength, altered mechanical properties, and sub-failure injury of the cervical spine ligaments. These injuries can affect the embedded mechanoreceptive and nociceptive nerve endings, resulting in pain, inflammation, and chronic symptoms. Therefore, ligamentous injuries in the cervical spine could contribute to persistent symptoms after a whiplash injury (Elliott et al., 2009).

Besides, injuries to the upper cervical ligaments can have a significant impact on the development of WAD symptoms (Krakenes et al., 2002). Studies using high-resolution MRI have demonstrated high signal intensity in the alar and transverse ligaments and tectorial membrane in some people with WAD, indicating damage (Krakenes et al., 2002). Furthermore, other research has found a significant correlation between the severity of alar ligament damage and the replication of pain as well as increased mobility during the manual examination of upper cervical ligaments (Kaale et al., 2008). These results indicate that injuries to the upper cervical ligaments may play a role in the development of WAD symptoms.

1.2.2.3 ***Facet joints***

The facet capsular ligament is relatively weak, and the facet joint can experience abnormal motions during whiplash, resulting in pain generation under certain loading conditions (Igarashi et al., 2007, Igarashi et al., 2004, Anderson, 2001). Therefore, cervical facet joints and their capsular ligaments have the potential to contribute to pain and dysfunction in individuals with whiplash injury (Igarashi et al., 2007, Igarashi et al., 2004, Anderson, 2001).

Clinical studies suggest that structural damage in the facet joint may be a possible cause of symptoms in individuals with WAD. Provocative testing and anaesthetic nerve blocks have implicated the facet joint as the primary source of pain in 25-62% of cases (Bogduk, 2011, Aprill and Bogduk, 1992). In a study of 128 patients with chronic neck pain, 82 were completely relieved of pain after undergoing diagnostic blocks to the cervical facets (Aprill and Bogduk, 1992). Lord et al. (1996) found that, in a placebo-controlled trial, zygapophyseal joint blocks significantly reduced pain in a proportion of patients with chronic

WAD. Furthermore, radiofrequency neurotomy, which disrupts the medial branches that innervate the cervical facet joints, has been shown to relieve pain symptoms (Bogduk, 2011). These results suggest that facet joint dysfunction may be a possible explanation for pain in these patients.

1.2.3 Classification of WAD

The Quebec Task Force (QTF) developed a classification system in which patients with WAD can be classified into five categories based on signs and symptoms (Table 1.1) (Spitzer et al., 1995). This classification has been adopted extensively in the WAD literature (Spitzer et al., 1995). At least 70% of WAD patients have grade II, which is the most common grade (Williamson et al., 2015). Individuals with WAD grade II are at risk of developing persistent symptoms (Agnew et al., 2015). Although most patients with WAD fall into the grade II classification, one problem outlined with this classification is that it does not capture all ranges of physical impairments and does not consider the psychological disturbances seen in people with WAD (Sterling, 2004).

Table 1.1: Classification of WAD

Grade	Criteria
0	No complaints about the neck and no physical signs
I	Complaint of neck pain, stiffness or tenderness only with no physical signs
II	Neck complaint and musculoskeletal signs, such as decreased range of motion and point tenderness
III	Neck complaint, musculoskeletal and neurological signs
IV	Neck complaint and fracture or dislocation

Sterling (2004) proposed a conclusive classification system that considers measurable dysfunctions related to motor, sensory and psychological function in people with acute WAD.

A summary of the proposed classification is presented in Table 1.2. A major difference between this classification and the one developed by QTF is that Sterling (2004) reclassified grade II into further sub-classifications (A, B and C). This classification system allows for the inclusion of identified impairments linked to sensory, motor and psychological disturbances in patients with WAD, and thus provides a more comprehensive approach reflecting the complexity of this disorder (Sterling, 2014). However, due to its greater complexity, the developed system has not been adopted by all stakeholders engaged in managing patients with WAD (Sterling, 2014).

Table 1.2: Proposed new classification system for acute whiplash associated disorders

Grades	Criteria
0	• No complaint about neck pain • No physical signs
I	• Neck complaint of pain, stiffness or tenderness only • No physical signs
IIA	• Neck pain • Motor Impairment o Decreased ROM o Altered muscle recruitment patterns (CCFT) • Sensory Impairment o Local cervical mechanical hyperalgesia
IIB	• Neck pain • Motor Impairment o Decreased ROM o Altered muscle recruitment patterns (CCFT) • Sensory Impairment o Local cervical mechanical hyperalgesia • Psychological impairment o Elevated psychological distress (GHQ-28, TAMPA)
IIC	• Neck pain • Motor Impairment o Decreased ROM o Altered muscle recruitment patterns (CCFT) o Increased JPE • Sensory Impairment o Local cervical mechanical hyperalgesia o Generalised sensory hypersensitivity (mechanical, thermal, BPPT) o Some may show SNS disturbances • Psychological Impairment o Psychological distress (GHQ-28, TAMPA) o Elevated levels of acute posttraumatic stress (IES)
III	• Neck pain • Motor Impairment o Decreased ROM o Altered muscle recruitment patterns (CCFT) o Increased JPE • Sensory Impairment o Local cervical mechanical hyperalgesia

	o Generalised sensory hypersensitivity (mechanical, thermal, BPPT) o Some may show SNS disturbances • Psychological Impairment o Psychological distress (GHQ-28, TAMPA) • Elevated levels of acute posttraumatic stress (IES) • Neurological signs of conduction loss including: o Decreased or absent deep tendon reflexes o Muscle weakness o Sensory deficits
IV	• Fracture or dislocation

Reprinted from Manual Therapy, 9(2), Michele Sterling, A proposed new classification system for whiplash-associated disorders—implications for assessment and management, 60-70, Copyright Elsevier (2004), with permission from Elsevier. Permission is available in Appendix 7.

1.3 Clinical manifestations of WAD (acute, chronic, and recurrent stages)

Following a whiplash injury, individuals often present with a myriad of signs and symptoms. Neck pain and headache are among the most common symptoms (Al-Khazali et al., 2020). When there is neck pain, it occurs within 6 hours in 65% of patients, within 24 hours in 93% and within 72 hours in 100% of patients (Deans et al., 1986). Neck pain following a whiplash injury is associated with poorer health-related quality of life (Kumagai et al., 2021), and a negative impact on work ability, physical performance and family and psychological functioning (van Randeraad-van der Zee et al., 2016). Other symptoms following whiplash trauma include temporomandibular joint dysfunction, auditory and visual dysfunctions, dysphagia, dysphonia, difficulty concentrating, memory loss, fatigue and dizziness (Elliott et al., 2009). Furthermore, specific deficits related to psychological distress, movement dysfunction, sensorimotor disturbances and neuromuscular adaptations are found in individuals following a whiplash injury.

1.3.1 Psychological manifestations

Some individuals with WAD have been shown to exhibit a variety of psychological characteristics, including depression, distress and post-traumatic stress disorder (Al-Khazali et al., 2022). For example, depression is reported in approximately 33% of individuals with WAD at 6 months post-injury (Al-Khazali et al., 2022). In addition, post-traumatic stress disorder has been reported to affect up to 16% of individuals with WAD (Al-Khazali et al., 2022). The presence of post-traumatic stress disorder has been shown to predict poor functional recovery (Campbell et al., 2018).

A large number of people with chronic pain who relate their symptoms to trauma, such as motor vehicle accidents, are afraid to engage in activities that they feel would either cause more harm or intensify their symptoms (Robinson et al., 2013). The fear-avoidance model of pain was introduced, which considers how catastrophising and negative beliefs affect patient's behaviour and illness recovery (Vlaeyen et al., 1995b). This model proposes that fearful individuals frequently engage in activities aimed at escaping or avoiding unpleasant stimuli and become hypervigilant to cues connected to fearful situations (Kasch et al., 2016). Two psychological variables are included in the fear-avoidance model: kinesiophobia and pain catastrophising.

Kinesiophobia is defined as an exaggerated, unreasonable and incapacitating fear of performing a certain movement or activity owing to a sense of susceptibility to receiving a painful injury or reinjury (Kori, 1990). The most consistent psychological features related to neck pain problems appear to be fear-avoidance beliefs and kinesiophobia (Karlsson et al., 2016, Robinson et al., 2013). In many studies, kinesiophobia and pain catastrophising have been found to have a negative impact on the onset and maintenance of chronic pain in people with WAD (Martinez-Calderon et al., 2020).

Pain catastrophising is defined as a series of exaggerated and ruminating negative cognitions and emotions that occur in response to an actual or imagined painful stimulus (Leung, 2012). It appears to be a more common trait when pain is caused by trauma, such as in a car accident (Margiotta et al., 2017). Greater degrees of pain catastrophisation in these individuals may have an impact on their ability to return to work (Carriere et al., 2015) and can be associated with enhanced pain and disability and poor mental health (Sullivan et al., 2002). On the positive side, a 10-week rehabilitation programme targeting psychosocial obstacles resulted in a significant reduction in pain catastrophising, which led to a greater return to work rate for people with WAD (Sullivan et al., 2006).

1.3.2 **Movement dysfunction in WAD**

1.3.2.1 ***Range of Motion***

The assessment of active cervical range of motion (ROM) in patients with neck pain is extensively used as a clinical tool and outcome measure (Stenneberg et al., 2017). Such a measure has been utilised by physiotherapists and other health care providers for describing patients' impairments in cervical mobility, investigating its prognostic ability and assessing the effects of physiotherapy interventions (Snodgrass et al., 2014).

Patients with WAD frequently present with restricted neck mobility and limited ROM has commonly been observed in patients soon after a whiplash injury (Fernández-Pérez et al., 2012). Similarly, a previous review has shown that such limited cervical mobility is also observed in patients with chronic WAD (Stenneberg et al., 2017), chronic idiopathic neck pain (Moghaddas et al., 2022) and headaches (Liang et al., 2019). Restricted cervical mobility is shown to be associated with activity limitations, neck pain and neck disability in patients with chronic neck pain (CNP), either idiopathic or traumatic (Rudolfsson et al., 2012). However, although ROM was evidently reduced during the acute and chronic stages (Fernández-Pérez et al., 2012, Stenneberg et al., 2017), this has not been investigated in people with recurrent neck pain (RNP) during remission, whereas individuals with WAD are pain free.

1.3.2.2 ***Velocity and smoothness of movement***

During daily activity, dynamic neck movement characteristics are functionally important (Röijezon et al., 2010). For instance, quickly turning the head to scan the visual field when walking or driving or in response to a sound, touch or even smell is important (Bahat et al., 2016). Velocity and smoothness of movement are shown to be valid measures for assessing people with neck pain disorders (Röijezon et al., 2010), with high sensitivity and specificity (Bahat et al., 2015a), in individuals with chronic WAD. Smoothness of movement refers to the fluidity and consistency of a movement (Robertson et al., 2013). Smooth movement is characterised by a continuous and uninterrupted motion with no jerky or abrupt changes in direction or speed (Robertson et al., 2013). Smoothness of movement can be quantified in different ways such as by calculating the number of velocity peaks (NVP) during a movement (Bahat et al., 2010). Lower NVP indicates smoother motion and better performance (Bahat et al., 2014b).

A study found that maximum angular velocity and acceleration were altered in people with chronic WAD when performing continuous flexion-extension movement than in healthy controls (Baydal-Bertomeu et al., 2011). The same findings were seen in cohorts of individuals with both chronic WAD and insidious neck pain who presented with a slow velocity of neck motion during cervical flexion and extension (Vikne et al., 2013) and irregular neck motion during left cervical rotation (Sjölander et al., 2008). These impaired cervical kinematics were found to be associated with dizziness and fear of neck movement (Takasaki et al., 2013). The presence of slow and irregular neck movements following a whiplash injury or during remission in people with pain recurrence is still unknown and has not yet been studied. However, evidence from other populations with musculoskeletal disorders indicated that reduced velocity of movement during rotation was observed, even during remission from neck pain, in people with concussions (Galea et al., 2022), and irregular neck movement was observed in people with recurrent low back pain (LBP) (Viggiani et al., 2020). Knowledge about this may be useful for informing clinical examinations of individuals with WAD and for developing novel interventions to target movement dysfunction.

1.3.3 Sensorimotor disturbances

Unsteadiness or dizziness (Treleaven et al., 2003), visual disturbances (Tjell et al., 2002) and loss of balance (Treleaven et al., 2005b) are frequently reported in individuals with persistent WAD. Other disturbances in balance, postural control (Treleaven et al., 2005b) and oculomotor control (Treleaven et al., 2011) have also been observed in a large number of people with chronic WAD.

Half of individuals with WAD have reported vision problems following whiplash trauma that caused problems during reading and a greater sensitivity to light (Treleaven and Takasaki, 2014). Eye movement dysfunction was more severe in WAD patients who experienced dizziness (Treleaven et al., 2005a). Impaired postural stability has also been observed in subjects with traumatic neck pain (Bianco et al., 2014), particularly when standing on a small base of support with their eyes closed (Treleaven, 2017).

Cervical proprioception assessed by head repositioning to a neutral position (e.g. Joint Position Error [JPE], as shown in Figure 1.3) has been assessed frequently in individuals with WAD. Greater JPE compared to healthy controls was seen in individuals with chronic WAD when the head was relocated to a neutral head position following cervical rotation (Mazaheri et al., 2021). Similarly, impaired cervical proprioception was also seen soon after a whiplash injury (Sterling et al., 2003b) which was greater in people with acute WAD compared to healthy controls. In non-traumatic cohorts, neck proprioception was able to differentiate between people with recurrent pain episodes and healthy controls (Elsig et al., 2014). However, to the best of my knowledge, neck proprioception has not previously been investigated in people with recurrent episodes of neck pain following a whiplash injury.

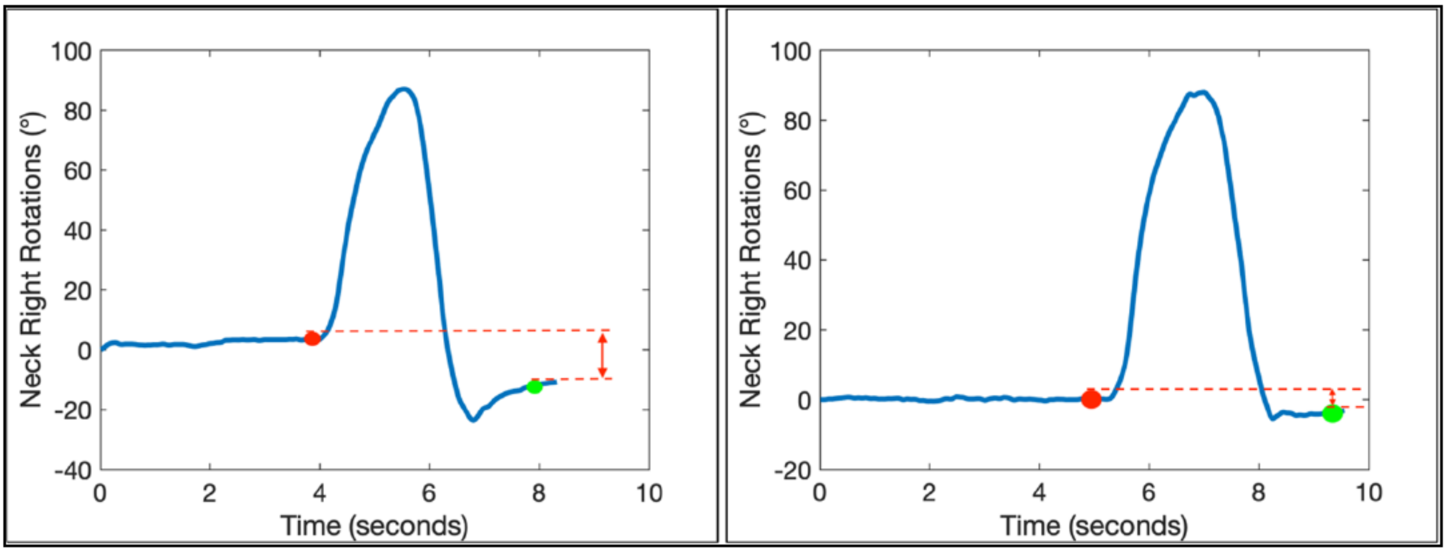

Figure 1.3: Cervical rotation plots in people with acute whiplash injury (left) and healthy controls (right) during a neck proprioception task. Joint position error (JPE) is defined as the vertical difference between the initial head location (red circle) and the target location (green circle). People with neck pain presented with a higher JPE than healthy controls.

Several factors can affect the extent of altered cervical proprioception in people with WAD. Dizziness or greater pain intensity are common symptoms of chronic WAD, and individuals with WAD typically exhibit greater sensorimotor control impairments than non-traumatic populations (Treleaven, 2011). A recent systematic review by Mazaheri et al. (2021) involving participants with WAD confirmed this finding, as individuals with dizziness performed worse on cervical repositioning tasks than those with no dizziness.

1.3.4 Neuromuscular adaptations in the presence of pain

1.3.4.1 ***Muscle strength***

Regardless of the cause of neck pain, such patients frequently have weaker neck muscles than healthy controls (Pearson et al., 2009, Lindstroem et al., 2012). The level to which neck strength is decreased in those suffering from neck discomfort varies greatly, with findings ranging up to a 90% reduction in strength when compared to healthy people (Prushansky et al., 2005). Neck strength in patients with acute WAD was assessed when perfuming isometric flexion and extension within one week of injury (Krogh and Kasch, 2018). At all time points (7, 30, 100, 180 and 365 days), the group with acute WAD displayed reduced cervical strength in both directions compared to people with an acute ankle injury. After one year, however, there were no significant differences in flexion (Krogh and Kasch, 2018). In patients with chronic WAD, Pearson et al. (2009) found significantly lower isometric neck force compared to healthy controls in cervical extension, retraction and left lateral flexion. This, however, has not been investigated in people with recurrent episodes of neck pain.

1.3.4.2 ***Endurance and fatigue***

Spatial reorganisation of muscle activity during contractions is an essential neural strategy because it efficiently distributes a load so that no one tissue or structure is overloaded (Jull et al., 2018). This is possibly significant in preventing overloading the same muscle fibres during extended activation, which can reduce muscle fatigue and increase muscle endurance (Farina et al., 2008). For example, by using high-density electromyography, a study showed that when healthy individuals perform sustained shoulder abduction, the activity within the upper trapezius muscle shifts towards the cranial area of the upper trapezius muscle (Falla et al., 2010a). This was seen as a change in the centroid of activity of the high-density EMG amplitude map towards the cranial region. This change in the distribution of activity within the muscle may prevent continuous loading of one tissue or structure. However, in the presence of pain, there is less redistribution of activity to different muscle regions (Falla et al., 2010a).

Multiple investigations have revealed poor endurance of the neck flexors, extensors and craniocervical flexor muscles in individuals with neck pain (Edmondston et al., 2011, O’Leary et al., 2007). Edmondston et al. (2011) assessed the endurance of neck flexors and extensors in individuals with postural neck pain during a sub-maximal isometric endurance test. The study did not find significantly lower endurance, assessed by time to task failure, of the neck extensors in people with neck pain compared to the control group. However, observations of poor endurance were seen in another cohort of people with a history of neck pain (O'Leary et al., 2007). In this study, the endurance of the craniocervical flexor muscles was assessed at 50% and 20% of the maximum voluntary contraction (MVC) during the performance of a cranio-cervical flexion (CCF) test (O'Leary et al., 2007). The study found a significant reduction in the ability to sustain craniocervical flexor contractions in people with neck pain compared to the controls, indicating deficits in endurance in these muscles. A similar observation of poorer endurance in neck flexors was found in people with traumatic neck pain compared to healthy controls (Dumas et al., 2001).

In addition to deficits in the endurance of neck muscles, poor steadiness of contraction was also seen in individuals with chronic idiopathic neck pain at a light load (20% of MVC) (O'Leary et al., 2007). Participants had to accurately maintain a 20% MVC level of contraction effort during the performance of CCF test until they felt that their muscles could no longer sustain the contraction. To determine the contraction's accuracy, the proportion of recorded samples that remained within a predetermined amplitude margin (3%) was used (O'Leary et al., 2007). The study found that people with neck pain have significantly poorer accuracy in maintaining steady low-load contraction at their 20% MVC compared to healthy controls (O'Leary et al., 2007). Additionally, reduced force steadiness was also observed in women with chronic and idiopathic neck pain when performing brief constant force contractions and circular contractions (Falla et al., 2010b, Muceli et al., 2011). When fatigue was assessed subjectively using Borg's scale (Borg, 1982), the same findings of greater perception of fatigue compared to healthy controls were seen in individuals with cervical radiculopathy (Halvorsen et al., 2014) and those with recurrent LBP (D'hooge et al., 2013).

1.3.4.3 ***Muscle coordination***

The neck contains 44 muscles that work together to support and control the cervical spine and allow for voluntary movements (Jull et al., 2018). The central nervous system handles the complex anatomy of the neck muscles by creating consistent muscle combinations to produce multi-directional forces (Gizzi et al., 2015, Grieve, 2004, Keshner and Peterson, 1988). Neck muscles have typical preferred directions of activation based on their position in relation to the spine, which helps optimise their recruitment for specific movements or tasks (Falla et al., 2010b, Blouin et al., 2007, Vasavada et al., 2002). This directional specificity in the recruitment of neck muscles for a specific action might be altered when actual or anticipated pain is present (Jull et al., 2018).

Reduced directional specificity of neck muscle activity was seen in individuals with persistent WAD when performing isometric contractions (Schomacher et al., 2012). Schomacher et al. (2012) investigated the activity of the deep semispinalis cervicis muscle in individuals with neck pain due to trauma. The study found that, unlike healthy controls, patients with chronic neck pain had reduced and less defined activity of the semispinalis cervicis muscle during multi-directional isometric contractions.

The cranio-cervical flexion is the primary action of the longus capitis and the longus colli muscles (Jull et al., 2008b), which can be assessed using the CCF test. To perform this test, subjects are positioned supine and asked to perform cranio-cervical flexion in progressive ranges of motion (Jull, 2000). The deep neck flexors, longus capitis and longus colli, are activated during craniocervical flexion, with minimal involvement from the superficial neck flexors and the SCM muscles (Falla et al., 2004d). Jull et al. (2004) assessed SCM activity in individuals with chronic WAD during the CCF test. When compared to the control participants, the group with WAD demonstrated greater activity of the SCM during each step of the test (Jull et al., 2004). Similarly, in individuals with acute WAD, the activity of the superficial neck flexors was also greater compared to healthy controls (Sterling et al., 2003b). This greater activity was maintained when assessed three months later in the WAD group during the performance of this CCF test (Sterling et al., 2003b). It has been demonstrated that increased activation of the superficial neck flexors during this test indicates reduced activity of the deep cervical flexors (Jull and Falla, 2016). Further studies are needed to confirm these findings and whether such adaptations exist in people with RNP during the remission of pain and to assess their predictive capacity.

Similar findings of muscular adaptations in neck extensors in people with neck pain were reported previously (Jull et al., 2008a). A study conducted by Nederhand et al. (2000) found that individuals with chronic WAD had higher coactivation levels than healthy controls in the upper trapezius muscle during and after movement. Additionally, the upper trapezius muscle has been observed to have a reduced ability to relax after repetitive arm movements, a decreased rest period during repetitive tasks, and is more likely to become active during mentally demanding tasks, as seen in various studies (Fredin et al., 1997, Falla et al., 2004a, Nederhand et al., 2000, Hägg and Åström, 1997, Veiersted et al., 1990, Laursen et al., 2002).

Besides increased muscle activity of superficial neck muscles, the presence of trigger points in individuals with acute WAD was examined previously (Fernández-Pérez et al., 2012). Trigger points are defined as hyperirritable spots within a taut band of skeletal muscle fibres that are painful on palpation and may lead to referred pain or other symptoms (Travell and Simons, 1992). They can be classified as active or latent (Travell and Simons, 1992). When stimulated, active trigger points mimic the patient's symptoms, and the patient experiences the pain as being familiar. Latent trigger points exhibit identical findings to the active ones, but they do not reproduce the patient's symptoms. A study found a significantly higher number of active and latent trigger points in the upper trapezius muscles, SCM, and levator scapulae in people with acute WAD compared to healthy controls (Fernández-Pérez et al., 2012). Specifically, the mean numbers of active and latent trigger points were 3.9±2.5 and 3.4±2.7, respectively, in patients with acute WAD. Healthy controls had no active trigger points but only presented with an average number of 1.7±2.2 latent trigger points. Similar findings of prevalent trigger points located in the upper trapezius, levator scapulae, SCM, and masseter muscles were also seen in people with WAD (Ettlin et al., 2008). A summary of common clinical manifestations of physical features in people with WAD during different pain stages is summarised in Figure 1.4.

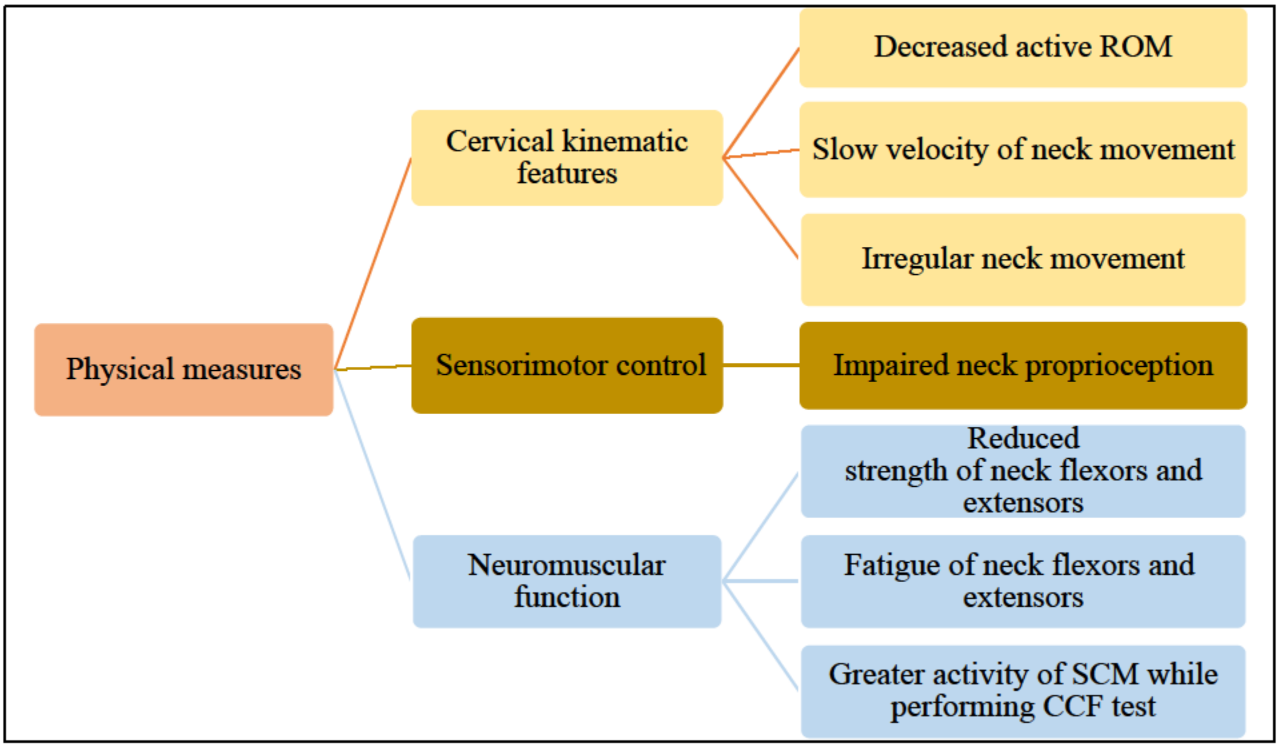

Figure 1.4: A summary of common physical features in people with neck pain following a whiplash injury.

1.3.4.4 The need for prediction of features related to movement and neuromuscular function[1]

There has been little investigation of the predictive utility of movement and neuromuscular function following a whiplash injury; of the studies conducted, measures of movement and neuromuscular function have been limited to measures such as ROM (Kasch et al., 2008) and CCF test performance (Falla et al., 2004d). However, features related to cervical movement and neuromuscular function may offer the potential to improve prediction accuracy. For example, decreased maximum angular velocity of neck movements has been observed in individuals with chronic WAD when compared to healthy individuals (Baydal-Bertomeu et al., 2011). Such changes in movement behaviour have been confirmed in individuals with WAD and insidious neck pain, where lower peak velocity was observed in both groups (Sjölander et al., 2008). In addition, a significantly larger jerk index (a measure of the smoothness of neck movement) has been reported in individuals with CNP of both insidious and traumatic onset when compared with asymptomatic individuals (Sjölander et al., 2008). Another feature reported by patients with CNP was increased coactivation of the neck flexors and extensors (Fernandez-de-las-Penas et al., 2008), which was associated with reduced neck strength (Fernandez-de-las-Penas et al., 2008). These additional features have not been investigated in individuals with acute WAD, but results from experimental pain studies suggest that these adaptations occur soon after pain onset and may therefore have relevance for ongoing symptoms in individuals with chronic WAD (Falla et al., 2007a, Madeleine et al., 2006, Madeleine et al., 2008, Muceli et al., 2014, Smith et al., 2005, Tucker and Hodges, 2010, Hug et al., 2014, Gizzi et al., 2015).

[1] This section (1.3.4.4) reports the contents of a published manuscript by the thesis author (Alalawi et al., 2020). It includes verbatim text from the published manuscript and some changes employed for the purpose of this thesis.

1.3.5 Predictive factors of transition from acute pain to chronicity in WAD

In individuals with WAD, several predictive factors have been studied, including social, psychological and physical factors, which are described below.

1.3.5.1 ***General patient characteristics including previous musculoskeletal pain***

The predictive capacity of demographics, such as age, gender and education for people suffering from WAD, was assessed in previous studies (Walton et al., 2013b, Sarrami et al., 2017, Walton et al., 2013a). The pooled size effect of the cohorts found that female gender and lower education were significantly associated with pain and disability in patients with acute WAD (Walton et al., 2013b). However, controversial evidence still exists regarding the association between age and persistent outcomes of WAD (Sarrami et al., 2017). Moderate evidence has found no association between old age and persistent pain and disability in people with WAD (Walton et al., 2013a).

The preinjury health of people with WAD has been studied (Kamper et al., 2008, Walton et al., 2013a), including factors such as neck pain, sick leave, widespread pain, headache, back pain, shoulder pain and use of pain medication. Three factors were found to be significantly associated with the outcomes of WAD, including prior neck pain, sick leave due to neck pain and prior headaches (Kamper et al., 2008). However, a meta-analysis found that a previous headache was not associated with the risk of persistent outcomes, even after removing the source of heterogeneity (Walton et al., 2013b). The same study found that prior neck pain increases the risk of persistent pain and disability in people with acute WAD, which was supported by moderate evidence from another meta-review by the same group of researchers (Walton et al., 2013a).

1.3.5.2 ***Psychosocial features***

A systematic review of psychological features and the development of poor outcomes in WAD provided inconclusive evidence (Williamson et al., 2008). Moderate evidence indicated that initially greater post-traumatic distress symptoms and catastrophising were risk factors for people with WAD developing persistent symptoms (Walton et al., 2013a). However, limited evidence has shown that post-injury lower self-efficacy (Williamson et al., 2008) and anxiety (Williamson et al., 2008, Carroll et al., 2008b) were associated with persistent WAD. However, controversial associations have been found between post-injury psychological factors and poor outcomes (Sarrami et al., 2017), including coping behaviour (Williamson et al., 2008, Carroll et al., 2008b), depression (Carroll et al., 2008b) and general psychological distress (Kamper et al., 2008).

1.3.5.3 ***Factors related to litigation***

Spearing et al. (2012) described the concept of injury compensation for road traffic crash victims, which can cover both economic and noneconomic losses and may provide access to health and rehabilitation services. Individuals who have sustained injuries in road traffic accidents can seek financial compensation to recover some or all of the losses they have incurred. This compensation can include compensation for both economic losses, such as lost wages, and noneconomic losses, such as pain and disability (Spearing et al., 2012). Furthermore, some compensation schemes also expedite access to healthcare and rehabilitation services or cover the costs of treatment. Spearing et al. (2012) argued that while it is expected that financial compensation would improve the well-being of injured individuals, there is evidence that the compensation-related factors involved in seeking and receiving compensation may lead to worse health outcomes, which is known as the compensation hypothesis (Spearing and Connelly, 2011).

The predictive ability of factors related to litigation was previously assessed in people with WAD (Spearing et al., 2012). These factors include the pursuit of compensation, the design of the compensation scheme, the involvement of lawyers, and the status of litigation. The study found a negative significant association between health outcomes and compensation factors in over half of the studies included in the review (Spearing et al., 2012). Other studies found that factors related to compensation were also associated with poor outcomes in people with WAD (Sarrami et al., 2017, Carroll et al., 2008b). However, it has been emphasised that it is unclear whether such significant associations reflect the compensation effect or if they are simply due to individuals who have worse health or a worse prognosis pursuing compensation, i.e., a selection effect (Spearing et al., 2012).

1.3.5.4 ***Injury characteristics***

1.3.5.4.1 Neck disability

A review found high-quality evidence that initially greater baseline disability was consistently associated with long-term pain and disability in people with WAD (Walton et al., 2013a). This association was established in another recent meta-review that confirmed such a relationship (Sarrami et al., 2017).

1.3.5.4.2 Onset of symptoms

The appearance and intensity of symptoms following whiplash trauma vary among patients. Some patients report symptoms immediately after the collision, while others take more than 24 hours to report symptoms (Sterling, 2010a). It was found that the onset of neck pain was not associated with neck pain and disability six months after a whiplash injury (Elrud et al., 2016).

1.3.5.5 ***Pain characteristics***

Many studies have been conducted to investigate baseline pain characteristics and prognoses following whiplash trauma. High-quality evidence indicated that initially greater baseline neck pain intensity was consistently associated with long-term pain and disability in patients with WAD (Walton et al., 2013a, Walton et al., 2013b). In addition, widespread pain is common in patients with WAD and is associated with poor outcomes (Falla et al., 2016).

1.3.5.6 ***Quantitative sensory testing***

Patients with acute WAD have widespread sensory hypersensitivity, including lower pain thresholds to cold, to mechanical or heat stimuli, than those who recover (Sterling et al., 2003a). Moderate evidence has shown that cold hyperalgesia is a prognostic factor in predicting poor prognosis in WAD patients (Walton et al., 2013a) and remains a significant outcome of WAD when controlling for possible covariates (Goldsmith et al., 2012). Cold hyperalgesia was also associated with psychological distress in patients with both acute (Rivest et al., 2010) and chronic WAD (Sterling et al., 2008). Only individuals categorised as having moderate to severe disability (≥ 30 on the Neck Disability Index (NDI)) were shown to have a lower pain threshold six months following a whiplash injury compared to the control group and other whiplash groups (recovered and mild disability) (Sterling, 2010a).

1.3.5.7 ***Physical factors***

As reported previously in Sections 1.3.2, 1.3.3, and 1.3.4, people with WAD commonly present with altered physical features related to movement, sensorimotor function and neuromuscular function. In this section, a summary of the predictive abilities of these factors will be summarised.

There is evidence of reduced cervical movement in individuals with acute and chronic WAD. Qualitative synthesis from systematic reviews of patients with WAD revealed limited evidence regarding the association between reduced cervical movement and ongoing disability (Scholten-Peeters et al., 2003, Williams et al., 2007, Daenen et al., 2013), whereas no such association was found in another review (Kamper et al., 2008). This was further demonstrated in a meta-analysis that examined the predictive value of restricted movement on poor outcomes (Walton et al., 2009).

In addition to ROM, the predictive capacity of neck muscle activity was also assessed in people with acute WAD. Sterling et al. (2003b) assessed the predictive capacity of the level of SCM activity during the performance of the CCF test. The study found no significant predictive ability of superficial neck muscles on neck pain and disability at six months (Sterling et al., 2005) or two to three years post injury (Sterling et al., 2006).

Contrary to the amount of evidence on the predictive ability of ROM, there is scarce evidence for other physical features. This includes the predictive ability of cervical velocity and smoothness of movement, neck flexor and extensor strength, endurance and fatigue in people with acute, recurrent and chronic WAD following a whiplash injury. Knowledge of this could provide more information about motor control disturbances (Baydal-Bertomeu et al., 2011) and could facilitate targeted interventions.

1.3.6 **Predictive factors of recurrent pain in people with WAD**

Previous evidence has shown that altered movement and neuromuscular function can exist during the complete remission of pain (Devecchi et al., 2021) and not only during painful episodes. For example, people with recurrent LBP demonstrated significantly restricted trunk movement and slower movement velocity compared to healthy participants during a cross-reaching task (Crosbie et al., 2013). Moreover, other changes in muscle function were observed in people with recurrent LBP during remission, including an altered trunk control strategy (Shih et al., 2021), reduced back muscle endurance (Johanson et al., 2011) and greater co-contraction of superficial trunk muscles (Suehiro et al., 2018).

Although there is evidence of the presence of physical adaptations in people with spinal pain, even during remission, their predictive ability has not yet been assessed. Predicting the clinical course of spinal pain, whether it persists, improves or relapses, is particularly important because it would help clinicians to match various clinical phenotypes to various interventions and guide clinical expectations of recovery (Liew et al., 2020b). To date, evidence about the prediction of pain recurrence in people with spinal pain is scarce. Only two studies presented data on predictive factors for LBP recurrence (Da Silva et al., 2017), however, none have addressed RNP. Da Silva et al. (2017) indicated that a history of previous episodes of pain was the only consistent factor that predicted future recurrence of pain in individuals with LBP. This finding was confirmed in another study (Machado et al., 2017). The predictive ability of other features, such as awkward sitting position and a longer time spent sitting, were assessed and their association with recurrence of LBP within the next 12 months has been observed (da Silva et al., 2019).

1.3.7 Current challenges of WAD

1.3.7.1 ***Recurrence of neck pain***

In general, recurrence of pain is common in individuals with neck pain, with a negative impact on quality of life (Nolet et al., 2015). Developing primary prevention programmes for dealing with pain recurrence is challenging, especially for spinal pain, where there is commonly no identifiable cause of symptoms (Hartvigsen, 2018). Secondary prevention, on the other hand, might significantly lower the financial and societal consequences of disability resulting from recurrence of pain (Shih et al., 2021). One barrier to improving secondary prevention is that the primary focus of the current model of care for people with neck pain is the relief of neck pain (Jull et al., 2018). Jull et al. (2018) argued that the prevention of recurrent episodes of pain is a vital patient-centred outcome that should receive more attention. This could be achieved by shifting the current focus of the model of care to functional and physical rehabilitation, aiming to reduce recurrence rates (Jull et al., 2018). The effectiveness of physical rehabilitation in reducing pain recurrence was assessed in people with LBP (Steffens et al., 2016). The risk of an episode of pain was reduced following an exercise programme alone or when combined with education (Steffens et al., 2016).

The development of effective intervention programmes is hindered by the lack of established predictive factors for future pain recurrence (Da Silva et al., 2017). One way to improve the precision of treatment is to first identify which features can predict poor outcomes (Riley et al., 2013), such as future episodes of neck pain and recurrence. This might be achieved through the comprehensive assessment of a variety of measures in people with RNP, including features related to neck movement, neuromuscular adaptations and psychological function. The presence of such features and their predictive capacity in people with trauma-related RNP has not been conducted before; therefore, this thesis aims to fill this gap.

1.3.7.2 ***Large variability in clinical manifestations***

The previous section 1.3 showed that individuals with WAD present with heterogeneous clinical manifestations involving different stages of acute, subacute and CNP. Because of the large variability of clinical manifestation, whiplash is one of the most controversial and expensive musculoskeletal problems to treat today, since it has been challenging to develop distinct pathoanatomical diagnoses (Elliott et al., 2009).

1.3.7.3 ***High transition rate from acute to chronic stage***

The high rate of transition from the acute stage to the chronic stage is another issue. About half of individuals with WAD continue to report symptoms a year after their injury, according to the Bone and Joint 2000–2010 Task Force on Neck Pain and Related Disorders (Carroll et al., 2008b). A high percentage of transition was also observed in a study in which the chronicity rates ranged from 15–84% (Kyhlbäck et al., 2002). Chronic WAD is a treatment-resistant condition with scant evidence of beneficial interventions (Teasell et al., 2010). Moreover, individual responses to specific interventions vary greatly, as seen in a study in which as many as 44% of individuals with chronic WAD reported a significant reduction in pain following a 12-week programme of specific neck exercise (Ludvigsson et al., 2015). Therefore, preventing the development of chronic WAD is crucial. To achieve this, the early detection of physical factors that increase the likelihood of developing chronic symptoms is important, as it allows for better treatment allocation among those at risk (Jull et al., 2011).

1.4 Modifications to the thesis from the initial plan

1.4.1 **Reducing the sample size due to the COVID-19 pandemic**

The COVID-19 pandemic severely disrupted the collection of data from the participants included in studies presented within this thesis. This resulted in a smaller sample size than anticipated, as described in Table 1.3.

Table 1.3: Changes made to the thesis as a result of the COVID-19 pandemic

Initial plan	Modifications
Chapter Two	
• 150 participants with acute neck pain following a whiplash injury were initially planned to be recruited	• Only 18 participants were recruited before the site got closed due to lockdown
Chapter Three	
• No impact on this chapter as it is a systematic review based on published papers	
Chapter Four	
• A prognostic analysis was planned to investigate the predictive ability of cervical kinematic features on ongoing pain and disability six months following a whiplash injury	• Instead of a prognostic analysis, a correlation analysis was used to assess the association between features of cervical kinematics and ongoing pain and disability six months after the injury because the sample size collected at baseline did not power a prognostic analysis
Chapter Five	
• 50 participants with RNP and 15 with CNP following a whiplash injury were planned	• These numbers could not be achieved as data collection was halted due to the lockdown in England; only 22 participants with RNP and 8 with CNP were recruited

1.4.2 Reducing the number of physical measures

Some of the objective measures were not feasible to collect for people with acute WAD, despite our intention to assess them. The main reason for not assessing was to avoid the aggravation of pain in people with acute WAD. Further details are provided in each chapter, but a summary of the collected or not collected measurements for each chapter is provided in Table 1.4.

Table 1.4: Summary of measurements collected in each chapter of this thesis

Measurements		Chapter Two		Chapter Five		
		Acute WAD	Healthy	RNP	CNP	Healthy
Self-reported measures	Neck pain and disability	✓		✓	✓	✓
	Neck pain intensity	✓		✓	✓	✓
	Catastrophising	✓		✓	✓	✓
	Kinesiophobia	✓				
	Recovery expectations	✓				
	Neck pain after movement	✓				
	Quality of life			✓	✓	✓
	Perceived exertion			✓	✓	✓
	Number of painful episodes			✓		
Objective measures	ROM	✓	✓	✓	✓	✓
	Vmean	✓	✓	✓	✓	✓
	Vpeak	✓	✓	✓	✓	✓
	NVP	✓	✓	✓	✓	✓
	JPE	✓	✓	✓	✓	✓
	CCF MVC	X	X	✓	✓	✓
	SCM activity during sub-maximum CCF	X	X	✓	✓	✓
	MVC flexion and Extension	X	X	✓	✓	✓

NDI: Neck Disability Index; NRS: numeric rating scale; VAS: visual analogue scale; NRS-ROM: neck pain occurring immediately after neck motion tasks; PCS: pain catastrophising scale; TSK: Tampa scale of kinesiophobia; EQ-5D: European quality of life – 5 dimensions.
ROM: range of motion; Vmean: mean velocity; Vpeaks: mean of peak velocity; NVP: number of velocity peaks; JPE: joint position error; CCF MVC: maximum craniocervical flexion strength; SCM: sternocleidomastoid; MVC: maximum voluntary contraction.
✓: Represents measures that were planned and collected.
X: Represents measures that were planned but not collected.
The blank cells in the table mean that there was no plan for collecting such data.

1.4.3 Changing the recruitment site from Birmingham, UK to Malaga, Spain

The recruitment of participants with acute WAD within this thesis was challenging even before the COVID-19 pandemic. The initial plan for recruiting individuals with acute WAD was to initially recruit patients who visited a trauma centre in Birmingham, UK. This is because we were aiming to recruit people who may have greater pain and disability, as they will likely have poor outcomes following injury, as confirmed by a previous review [3]. This would have allowed a greater number of patients with WAD to be recruited. Moreover, this would have improved the representation of patients with WAD. However, after applying for clearance to recruit such participants, this was deemed impossible. According to what we were informed, the best way to reach these patients was through the insurance companies. However, this proved to be difficult because the insurance companies didn't want us to interfere with the usual care approach.

Due to this, we were compelled to locate an alternate recruitment site that would provide us with direct access to individuals who had neck pain originating from whiplash injuries. Following discussion with long-term collaborators, at the University of Malaga, Spain a centre in Malaga was chosen. Comprehensive details about the methods, recruitment and data management are reported in Chapter Two and are available in our published protocol (Alalawi et al., 2020).

1.5 Thesis aims and objectives

1.5.1 Aims

The overall aim of this thesis was to investigate the presence of altered cervical kinematics, neuromuscular function and psychological function in individuals with acute, recurrent and CNP following a whiplash trauma and to investigate their relevance for ongoing pain and disability in individuals with acute WAD and RNP.

1.5.2 Objectives

The objectives for each chapter in this thesis are as follows and are illustrated in Figure 1.5.

Chapter Two: To determine if features of cervical kinematics are altered in people with acute WAD and to examine whether such features are associated with self-reported outcomes.

Chapter Three: To systematically synthesise the current evidence regarding the predictive ability of features of physical function on ongoing pain and disability following a whiplash injury.

Chapter Four: To investigate the association between features of cervical kinematics collected at baseline and ongoing pain and disability six months after a whiplash injury.

Chapter Five: To examine whether there are any differences in features of cervical kinematics, neuromuscular function and psychological function in individuals with RNP or CNP following a whiplash trauma compared to healthy controls (cross-sectional design) and to investigate the predictive ability of such features in those with RNP (longitudinal design).

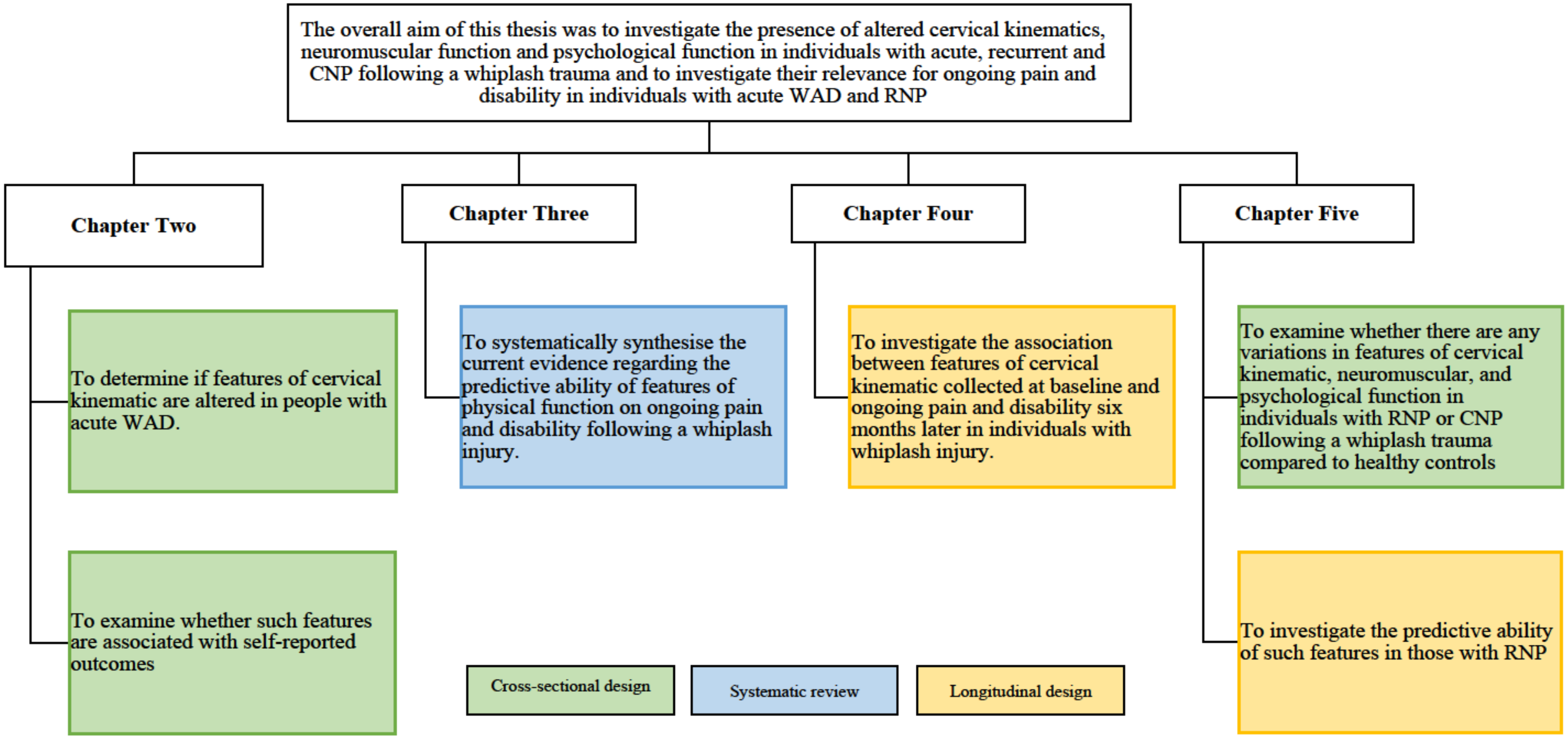

Figure 1.5: Objectives of each chapter in the current thesis

CHAPTER 2

PERCEIVED PAIN AND DISABILITY BUT NOT FEAR OF MOVEMENT ARE ASSOCIATED WITH ALTERED CERVICAL KINEMATICS IN PEOPLE WITH ACUTE NECK PAIN FOLLOWING A WHIPLASH INJURY

This chapter reports in full the contents of a published manuscript by the thesis author (Alalawi et al., 2022c). It includes verbatim text from the published manuscript and some changes employed for the purpose of this thesis to allow greater justification of methodological choices.

Publications and Presentations

4. **Alalawi, A.**, Fernandez-Sanchez, M., Devecchi, V., Gallina, A., Luque-Suarez, A. and Falla, D., 2021. People with acute neck pain following a whiplash trauma, present with reduced range, velocity and smoothness of neck movement. Physiotherapy UK 2020 Conference, Virtual.

6. **Alalawi, A.,** Luque-Suarez, A., Fernandez-Sanchez, M., Tejada-Villalba, R., Navarro-Martin, R., Devecchi, V., Gallina, A. and Falla, D., 2022c. Perceived pain and disability but not fear of movement are associated with altered cervical kinematics in people with acute neck pain following a whiplash injury. *Musculoskeletal Science and Practice*, p.102633. (**Appendix 4)**

2.1 ABSTRACT

The assessment of cervical kinematic features (e.g. velocity and smoothness of movement) besides ROM is of clinical importance as they may become targets for early intervention. Impaired dynamic cervical kinematics have been seen in people with chronic WAD, but they have not been examined in people with acute WAD. The aim of this study was to determine if measures of cervical kinematics are altered in people with acute WAD and secondarily, to examine whether kinematic variables are associated with self-reported outcomes.

This observational case-control study recruited people with acute WAD within 15 days after a motor vehicle collision and healthy control participants. All participants performed active neck movements at a self-determined velocity. ROM, peak and mean velocity of movement, smoothness of movement, and cervical JPE were assessed. Moreover, self-reported measures of perceived pain and disability, pain catastrophising, and fear of movement were obtained.

Sixty people participated: 18 with acute WAD (mean age [SD] 38.7 [12.0]) and 42 as asymptomatic controls (mean age [SD] 38.4 [10.2]). Participants with acute WAD showed significantly decreased ROM in all movement directions ($p<0.0001$). Participants with acute WAD showed a reduction in the mean and peak velocity of movement in all directions ($p<0.0001$) and the number of velocity peaks was significantly higher (i.e., reduced smoothness of movement) in those with acute WAD in all directions ($p<0.0001$). Repositioning acuity following cervical rotation was not significantly different between groups. Neck pain-related disability showed the largest number of significant associations with kinematic features, while fear of movement was not associated with cervical kinematics.

Participants with acute WAD presented with altered cervical kinematics compared to asymptomatic participants. Several measures of cervical kinematics were associated with the level of pain and disability in people with acute WAD but not their fear of movement.

2.2 INTRODUCTION

One of the most frequently measured physical signs in people with WAD is ROM and several studies report reduced ROM as a common feature in patients with acute (Fernández-Pérez et al., 2012, Kasch et al., 2001c, Kumbhare et al., 2005, Sterling et al., 2004) and chronic (Woodhouse and Vasseljen, 2008a, Sjölander et al., 2008, Armstrong et al., 2005, Baydal-Bertomeu et al., 2011, Dall'Alba et al., 2001, Madeleine et al., 2004, Grip et al., 2007, Kaale et al., 2007, Klein et al., 2001, Ohberg et al., 2003, Pereira et al., 2008, Prushansky et al., 2006, Puglisi et al., 2004, Shahidi et al., 2012) WAD. In addition to ROM, dynamic kinematic measures of movement such as velocity and the smoothness of movement have also been used previously to quantify changes in cervical kinematics in people following a whiplash injury. The validity of both measures has been established for the assessment of patients with neck pain (Sjölander et al., 2008), and high sensitivity and specificity of the measures have been confirmed (Bahat et al., 2015a). Previous studies report that people with chronic WAD typically move their neck with slower velocity (Vikne et al., 2013, Grip et al., 2008, Ohberg et al., 2003) and perform irregular neck motion (Sjölander et al., 2008). However, despite the functional importance of quick and smooth movements (Takasaki et al., 2013, Tsang et al., 2013, Yan et al., 2000), these kinematic features have not been examined in people with acute WAD.

Besides physical impairments, people often present with a number of relevant symptoms following a whiplash injury, with neck pain being the most frequently reported (Al-Khazali et al., 2020). Initial high levels of disability (Scholten-Peeters et al., 2003, Williams et al., 2007, Kamper et al., 2008, Walton et al., 2009, Alalawi et al., 2019, Carroll et al., 2008b), as well as initial higher intensity of neck pain (Williams et al., 2007, Kamper et al., 2008, Carroll et al., 2008b, Walton et al., 2013b), have been identified as predictors of poor outcome following a whiplash trauma (Walton et al., 2013a, Sarrami et al., 2017), as reviewed in Chapter One, Sections 1.3.5.4.1 and 1.3.5.5 page 25. Additionally, psychological features such as pain catastrophising (Sullivan et al., 2002) and fear of movement (Vangronsveld et al., 2008) can be present and the former is associated with poor recovery following a whiplash injury (Shearer et al., 2020), as reviewed in Chapter One, section 1.3.5.2 page 24. Although the association between measures of cervical kinematics and subjective features such as pain, disability and fear of movement have been examined in people with chronic pain following a whiplash injury or chronic non-specific neck pain (Bahat et al., 2014a, Howell et al., 2012, Treleaven et al., 2016, Waeyaert et al., 2016), there is very limited knowledge on how cervical kinematics are modified in people with acute pain following a whiplash injury and whether any change is associated with subjective complaints.

Understanding how movement is affected in people with acute WAD and how this relates to their symptoms is of relevance as this would prompt specific assessment of specific cervical kinematic features besides ROM (e.g. velocity and smoothness of movement) in people with acute pain and these may become targets for early intervention.

2.2.1 Aims and hypotheses

The aim of this chapter was to determine if features of cervical kinematic and psychological function are altered in people with acute WAD. We hypothesised that: (i) people with acute WAD will present with altered cervical kinematics including changes in the range, speed and smoothness of their neck movements, and, (ii) that these kinematic variables will be associated with self-reported outcome measures in people with acute WAD. Knowledge from this study could provide preliminary evidence showing that specific movement disturbances exist soon after a whiplash injury, and this may prompt future studies to examine whether movement features are predictive of poor outcome. If movement disturbances prove to be relevant, they could become targets for rehabilitation to improve movement quality aiming to potentially mitigate the transition to chronic pain.

2.2.2 **Objectives**

1. To determine if features of cervical kinematic and psychological function are altered in people with acute WAD.
2. To examine whether features of cervical kinematics are associated with self-reported outcomes, including pain intensity, disability, fear of movement, catastrophising, and expectations of recovery.

2.3 MATERIALS AND METHODS

2.3.1 **Study design**

An observational case-control study was conducted to evaluate measures of cervical kinematic in patients with acute WAD compared to healthy participants. It was conducted and reported according to the guidelines of The Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) statement (Von Elm et al., 2014), with the STROBE checklist available in Appendix 8. A detailed protocol for this study was published prospectively (Alalawi et al., 2020). The project was approved by the Ethics Committee of the province of Malaga, Spain (#30052019, Appendix 9 and Appendix 10).

As reported previously in the general introduction of this thesis, section 1.4.3, page 32, the recruitment of individuals with acute WAD was initially planned to be conducted in Birmingham, UK. We attempted to contact patients through their insurance companies, but this proved to be difficult because the insurance company didn't want us to interfere with their usual care. Alternatively, a physiotherapy centre in Malaga, Spain, was found, to which most patients with whiplash injuries are referred by their insurance companies. This has allowed us to access patients directly and soon after the injury.

***2.3.2* Pilot study and reducing the number of measures**

In this chapter, a priori plan was in place to collect comprehensive measurements from individuals with acute WAD. This includes measures of cervical kinematic, neck proprioception, co-activations of neck muscles, and neck muscle force during isometric neck flexion and extension. However, only measures related to cervical kinematics and proprioception were collected in this chapter. In other words, measures related to co-contraction of neck muscles and maximal neck extension/flexion force (isometric contractions) were not collected in this chapter. The decision to remove these tasks was taken during the pilot study of the first three participants, where the maximum isometric contraction appeared to aggravate the participants' neck pain. Moreover, for measurements related to the co-contraction of neck muscles, the device used to collect muscle activity using EMG was not stable when patients performed these two tasks and was producing noisy signals. There were several issues that contributed to the noise in EMG signals. One of the main issues was that the cables of the EMG device kept producing noise when a participant was performing contractions. Another issue is that this study was collected in a clinical setting (a physiotherapy clinic), in which we could not control for environmental artefacts. Finally, signal processing techniques were used to reduce noise and improve the quality of the EMG signal, but they did not sufficiently improve the signals.

Therefore, the pilot study allowed us to ensure the burden was significantly minimised on the participants and that only data of high quality was collected.

2.3.3 **Participants**

2.3.3.1 ***Acute WAD eligibility***

A convenience sample of patients with acute WAD were recruited from a single private physiotherapy clinic in Malaga, Spain. They were invited to participate in the study if they were 18 years or older, involved in a recent (previous 15 days) motor vehicle crash, and experienced acute neck pain. Participants were also required to understand written and verbal Spanish. They were excluded if they were categorised as WAD grade IV (spine fractures or dislocations) (Spitzer et al., 1995), or if they lost consciousness during or after their whiplash injury (Cantu, 1992). Participants with a previous history of neck surgery (Crawford et al., 2004), neck injury, malignant spinal disorders, mental disorders (Rosenfeld et al., 2000, Rosenfeld et al., 2003), or regular use of analgesic medication prior to the injury due to chronic pain were also excluded.

2.3.3.2 ***Healthy participants eligibility***

Healthy participants for this group were recruited if they have no current neck pain and no history of neck or shoulder pain that required treatment from a healthcare professional.

2.3.4 **Recruitment**

Details of the recruitment process has been published before (Alalawi et al., 2020) and is summarised in Figure 2.1.

Participants were recruited from a single private physiotherapy clinic in Malaga, Spain. One designated physiotherapist working at the physiotherapy clinic manually checked electronic clinical records of all consecutive patients attending the clinic. Once an eligible patient was identified at the clinic, the designated physiotherapist contacted the patient to invite them to participate in the study; this invitation was conducted either in-person at the clinic or via telephone after patients have returned home from their clinic appointment. A verbal and written description of the study were provided during the invitation. Those patients interested in participating were invited to the clinic to undergo an initial study session where the researcher explained the study, provided a detailed information sheet (Appendix 11), and obtained written informed consent (Appendix 12). Once recruited, all participants were asked to complete a baseline self-reported questionnaire and then undergo physical testing. Participants were informed that they can withdraw from the study at any time, without having to provide a reason. They were also advised to carry on with their daily routines as usual.

The control group of healthy participants were recruited from a local community at the University of Malaga, Spain through advertisement.

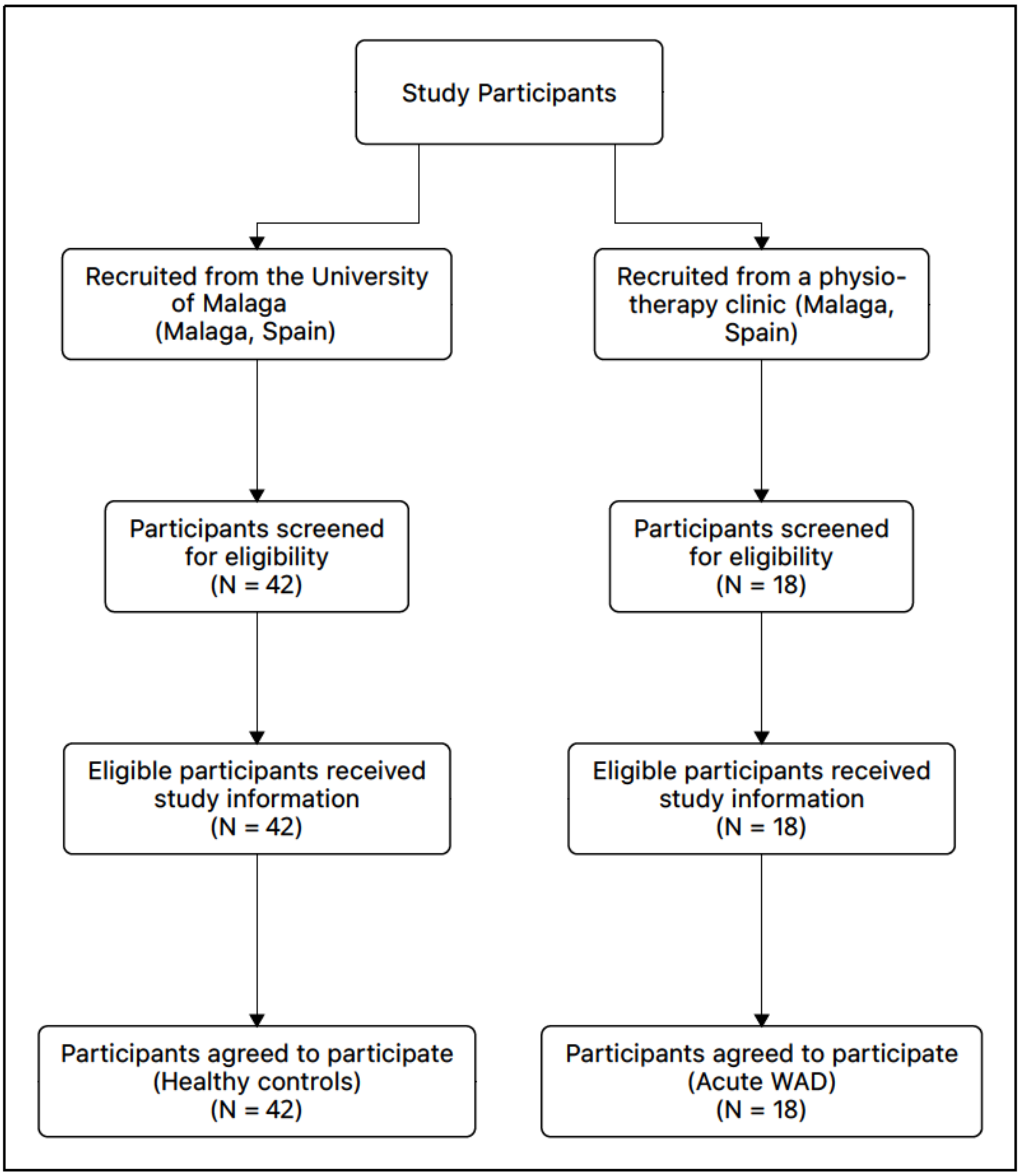

Figure 2.1: Flowchart of study population

2.3.5 Instrumentation

Cervical kinematic data was obtained using a wearable BTS G-WALK® sensor system (BTS Bioengineering, Italy), with a sampling rate of 100 Hz; an Inertial Measurement Unit (IMU) that is composed of a gyroscope, an accelerometer, and a magnetometer. It measures linear and angular characteristics of movement in three-dimensional space. The dimensions for the sensor are 70x40x18mm, and its mass is 37 grams. To collect kinematic data, the sensor was fixed on the participants' forehead using double-sided tape. The data were acquired with the G-Studio software (BTS Bioengineering, Italy). The G-WALK® sensor is a portable system that gives the position and orientation of the head, which allows various kinematic measures to be collected simultaneously including ROM, velocity profiles and the smoothness of motion; making it applicable in clinical practice and for research purposes, compared to other human motion analysis technology. The validity and reliability of G-WALK® sensor have been established albeit during gait, with an Intraclass Correlation Coefficient (ICC) ranging from 0.85 to 0.99 (De Ridder et al., 2019). Similarly, the concurrent validity of the G-WALK sensor for assessing spatiotemporal parameters during gait against a gold standard has been established in healthy participants (De Ridder et al., 2019, Vítečková et al., 2020).

2.3.6 Testing procedures

The main researcher (AA), who designed the protocol for this study, was not involved in the data collection for this project but only provided training for the assessor who performed the assessments. The data was collected independently by a designated physiotherapist who works at the clinic. Since both the recruitment and assessments of participants were conducted by the same physiotherapist, blinding was not possible.

Initially, all participants completed baseline self-reported outcomes, prior to physical data collection. Physical testing was then performed by a physiotherapist and consisted of the assessment of cervical kinematics including a measure of proprioception. Each test was carried out with the participated seated in a chair with their arms supported and their feet on the ground. The assessor fixed the sensor on the middle of participant's forehead and calibrated it to zero with the head in a natural position. Participants were then instructed to perform active neck movements as far as possible, at a self-paced natural speed, since most daily activity are performed at a natural speed (Bahat et al., 2010, Sjölander et al., 2008), and this is consistent with what has been described in previous studies (Meisingset et al., 2015, Salehi et al., 2021). The directions of the head movements were performed in the same order among participants. Although collecting physical measures in the same order could potentially introduce a training effect, several strategies were taken to minimise this risk within this study. Firstly, the purpose of the study was masked from all participants. Secondly, all participants were not aware of what was being measured during data collection. Finally, clear and concise instructions were given to the participants, explaining the procedures and tasks involved in the study.

Firstly, active neck flexion/ extension was performed by instructing the participant to look forward, then fully flex and extend their neck continuously and as far as possible without stopping until 5 cycles (trials) were completed. The choice of 5 cycles was chosen to generate a representative sample of data whilst minimising the risk of exacerbating the patients' symptoms. This number of repetitions was chosen, as it is similar to earlier studies that evaluated mobility in acute WAD patients (Sterling et al., 2003b). Similar procedures were applied for the active rotation task, whereby the participants performed 5 cycles of continuous right to left rotations. Participants were instructed to perform all movements in a pace that is similar to what they perceive as a normal speed (Sjölander et al., 2008).

Neck proprioception was then assessed and for this, participants performed three repetitions of right and left neck rotation. In each trial, the participants were instructed to memorise a self-selected neutral position (starting position), close their eyes, and perform active head rotation after which they should return to the starting position as accurately as possible. Each movement was repeated three times for both right and left rotation with a rest period of one minute between each movement.

2.3.7 Outcome variables

2.3.7.1 ***Patient reported outcome measures:***

Several self-reported outcomes were collected at baseline including disability, neck pain intensity, pain catastrophising, fear of movement, and recovery expectations in those with acute WAD. The used questionnaires, in Spanish, are available in Appendix 13, Appendix 14, and Appendix 15.

To assess neck pain and disability at baseline, the NDI (Vernon and Mior, 1991) was used. It consists of 10 items related to daily activities such as reading, lifting, driving, personal care, work, sleeping, and recreation (Vernon and Mior, 1991); each question has five ordinal response options from 0 (no disability) to 5 (complete disability). NDI scores were interpreted as recovered (NDI<8), mild pain and disability (NDI 10-28), moderate/severe pain and disability (NDI>30) (Sterling et al., 2005). The NDI is a valid and reliable measure in individuals with neck pain disorders (Lemeunier et al., 2019). The reliability of Spanish version of the NDI has been established (internal consistency Cronbach's α 0.89; intra-class correlation coefficient 0.98) (Andrade et al., 2008).

Current neck pain intensity was assessed using a NRS which is an 11-point scale range from 0 (no pain) to 10 (worst possible pain). Pain intensity using NRS was also assessed after patients had performed all neck movements testing (NRS-ROM). The reliability of NRS has been established in patients with neck pain (ICC:0.76) (Cleland et al., 2008).

Self-reported outcomes related to pain catastrophising was assessed using the Pain Catastrophising Scale (PCS) which consists of 13-item related to patients' rumination, magnification and helplessness about controlling their pain (Sullivan et al., 1995). It produces an overall score ranging from 0 to 52 with higher scores indicating greater pain catastrophising. PCS has been used to assess patients with WAD (Sterling et al., 2008, Sullivan et al., 2002), and its reliability and validity have been established (Sullivan et al., 1995). The Spanish version of PCS was used in this study (internal consistency Cronbach's α 0.79; test-retest reliability 0.84) (García Campayo et al., 2008).

The Tampa Scale of Kinesiophobia (TSK) (Roelofs et al., 2007) was used to assess fear of movement or injury during activities. It consists of 11-items producing a range score from 11 to 44 with (higher scores representing higher fear of movement). Scores greater than 37 is considered a high degree of fear of movement (Vlaeyen et al., 1995a). The reliability and validity of TSK have been established (Woby et al., 2005). The Spanish version of TSK was used in this study (internal consistency Cronbach's α 0.81 for people with acute pain) (Gómez-Pérez, 2011).

The evaluation of pain catastrophising and kinesiophobia in healthy controls was not considered in this study. Although comparing PCS and TSK scores between individuals with acute WAD and healthy controls could have offered some additional context, the focus was on understanding how these features relate to kinematic features in people with acute WAD.

A single question was asked to determine recovery expectations among patients; 'In your opinion, how likely is it that you will be fully recovered with no persistent sequelae?' (Elrud et al., 2016). Scores ranged between 0 ('not likely') and 10 ('very likely') to indicate how likely he/she will completely recover (Holm et al., 2008).

2.3.7.2 ***Objective outcome measures (features of cervical kinematic and proprioception)***

Data were analysed in Matlab (Mathworks Matlab 2019b). Signals were low pass–filtered (cut-off frequency of 10Hz; order: 10), as used previously (Sjölander et al., 2008). The start and end of the movement were defined as the time when the peak velocity passed the threshold of 5%, as used previously (Sjölander et al., 2008).

Maximum neck ROM (°) was defined as the maximum range achieved during each repetition of flexion, extension, right and left rotation. The mean value of the five repetitions for each direction was calculated and included in the analysis of this study.

Mean velocity (V*mean* [°/s]) was determined as the mean angular velocity achieved over the five repetitions for each movement direction. The average of the five values was included in the analysis for each movement direction.

Peak velocity (V*peak* [°/s])) refers to the maximal velocity value for each movement; the average of the five repetitions were included in the analysis for each movement direction.

NVP [n] refers to the number of times that the acceleration curve crossed zero. The average NVP that occurred across the five repetitions were combined and included in the analysis for each movement direction.

Cervical JPE [°] refers to the difference in degrees between the participants head position upon repositioning and the start location. The mean value of the three repetitions for each direction was calculated and included in the analysis.

2.3.8 Statistical analyses

Descriptive statistics between groups were performed for participant demographics, self-reported questionnaires, cervical kinematic features, and proprioception. The normality of data distribution for self-reported and objective outcomes was assessed using the Shapiro-Wilk Test. Based on the normality test, differences between groups were assessed using the independent t-test. Other variables such as mean velocity in extension and right rotation, peak velocity in flexion and rotations, NVP in flexion, extension, and right rotation, and JPE task in left rotation were not normally distributed and differences between groups were assessed using the Mann-Whitney U Test.

Bivariate correlations between self-reported outcome (NRS, NRS-ROM, NDI, TSK, PCS, recovery expectations) and objective measures were performed. Pearson's correlation coefficient was used if data was normally distributed, or Spearman's correlation coefficient if data were not normally distributed. Analyses were performed using SPSS 26.0 (IBM Corp., Armonk, NY, USA). Group differences were considered significant at the $p < 0.05$.

2.3.9 **Sample size**

In this study, sample size was estimated from similar research that examined the same spine kinematic characteristics which included 16 individuals with neck pain (Sjölander et al., 2008).

2.4 RESULTS

The baseline demographic characteristics of included participants in each group with their scores for the self-reported measures are summarised in Table 2.1. Results were analysed from a sample of 18 patients with acute WAD (14 women, 4 men, mean age 38.7 ± 12.0, mean BMI 25.2 ± 6.0), and 42 healthy controls (33 women, 9 men, mean age 38.4 ± 10.2, mean BMI 23.0 ± 3.8). No significant differences were observed between groups with regards to age (p=0.45), gender (p=0.95), or BMI (p=0.17). Self-reported questionnaires indicated that the patients presented with moderate/severe neck disability (mean NDI: 32.8±7.5, range 17-44), high neck pain intensity (mean NRS: 6.9±1.9, range 3-10), pain catastrophising (mean PCS: 21.4±19.8, range 0-52), moderate fear of movement (mean TSK: 33.4±9.6, range 11-44), but were mostly optimistic about their full recovery (mean recovery expectations: 8.0±2.1, range 3-10).

Table 2.1: Baseline characteristics

	Groups				p- value
	Acute (n=18)		Controls (n=42)		
	Mean (SD)	Median (IQR)	Mean (SD)	Median (IQR)	
Age (years)	38.7 (12.0)	38.0 (18.0)	38.4 (10.2)	38.5 (18.0)	0.45 [a]
Gender (women/men), n	14/4		33/9		0.95 [b]
BMI (kg/m^2)	25.2 (6.0)	23.2 (7.0)	23.0 (3.8)	21.6 (3.4)	0.17 [c]
NDI (0-50)	32.8 (7.5)	35.0 (11.0)			
NRS (0-10)	6.9 (1.9)	7.0 (3.0)			
NRS-ROM (0-10)	7.3 (1.6)	7.0 (2.0)			
PCS (0-52)	21.4 (19.8)	13.0 (41.0)			
TSK (11-44)	33.4 (9.6)	37.0 (14.0)			
Recovery expectations (0-10)	8.0 (2.1)	8.5 (3.0)			

SD: standard deviation; IQR: interquartile range; NDI: neck disability index; NRS: numeric rating scale; NRS-ROM: neck pain taking immediately after neck motion tasks; PCS: pain catastrophising scale; TSK: tampa scale of kinesiophobia
[a] Independent T-Test
[b] Pearson's Chi-squared test
[c] Mann-Whitney Test

2.4.1 Cervical kinematics

Summary statistics and differences between groups for maximal neck ROM, mean velocity, peak velocity, and JPE for both groups are presented in Table 2.2, and illustrated in Figure 2.2.

Table 2.2: Summary statistics and differences between groups

Kinematic Measures	Groups				Mean Diff	95% Confidence Interval of the Difference		Sig. (2-tailed)
	Acute		Controls					
	Mean (SD)	Median (IQR)	Mean (SD)	Median (IQR)		Lower	Upper	
Flexion								
ROM (°)	27.7 (15.0)	24.7 (24.3)	44.1 (12.7)	44.1 (21.1)	-16.4	-24.0	-8.8	**<0.001**
Vmean (°/s)	15.7 (9.7)	13.2 (14.7)	55.3 (14.6)	54.4 (19.7)	-39.6	-47.5	-31.7	**<0.001**
Vpeak (°/s)	41.3 (23.7)	35.1 (40.0)	107.2 (28.3)	104.5 (33.2)	-65.8	-81.4	-50.3	**<0.001[a]**
NVP (n)	49.0 (28.8)	47.0 (47.4)	14.2 (6.4)	12.4 (8.8)	34.8	25.5	44.1	**<0.001[a]**

(Continued)

Table 2.2: *(Continued)*

Kinematic Measures	Groups				Mean Diff	95% Confidence Interval of the Difference		Sig. (2-tailed)
	Acute		Controls					
	Mean (SD)	Median (IQR)	Mean (SD)	Median (IQR)		Lower	Upper	
Extension								
ROM (°)	29.7 (12.2)	26.9 (19.8)	51.9 (11.7)	52.6 (16.9)	-22.2	-28.9	-15.5	**<0.001**
Vmean (°/s)	17.6 (12.4)	12.6 (20.3)	55.0 (12.7)	57.1 (14.6)	-37.3	-44.6	-30.1	**<0.001**[a]
Vpeak (°/s)	44.3 (24.5)	40.3 (41.9)	108.1 (24.6)	103.8 (30.8)	-63.8	-78.1	-49.6	**<0.001**
NVP (n)	57.5 (32.8)	59.0 (55.7)	15.2 (6.8)	13.5 (8.0)	42.3	31.7	52.8	**<0.001**[a]
Right Rotation								
ROM (°)	42.9 (13.7)	44.8 (24.2)	59.0 (14.4)	60.6 (23.7)	-16.1	-24.4	-7.9	**<0.001**
Vmean (°/s)	26.1 (14.9)	23.3 (16.0)	83.2 (36.3)	76.4 (43.1)	-57.1	-75.4	-38.8	**<0.001**[a]
Vpeak (°/s)	71.2 (35.2)	64.8 (52.5)	186.9 (65.2)	171.2 (101.3)	-115.7	-149.5	-82.0	**<0.001**[a]
NVP (n)	42.9 (19.5)	40.5 (25.4)	12.6 (6.3)	11.5 (9.6)	30.3	23.6	37.1	**<0.001**[a]
JPE (°)	3.4 (2.1)	3.3 (3.2)	3.2 (2.1)	3.2 (2.7)	0.2	-1.1	1.4	0.39
Left Rotation								
ROM (°)	29.4 (8.7)	30.0 (9.5)	47.9 (15.3)	47.5 (22.9)	-18.5	-26.4	-10.5	**<0.001**
Vmean (°/s)	25.1 (16.2)	19.3 (18.2)	77.1 (26.5)	73.7 (30.9)	-52.0	-65.8	-38.1	**<0.001**[a]
Vpeak (°/s)	72.6 (39.1)	56.1 (48.0)	180.3 (70.3)	168.4 (82.4)	-107.7	-144.2	-71.2	**<0.001**
NVP (n)	47.3 (24.5)	40.2 (37.0)	12.9 (5.7)	11.2 (7.5)	34.4	26.2	42.6	**<0.001**
JPE (°)	3.8 (2.4)	3.1 (3.3)	3.1 (2.6)	2.5 (2.6)	0.7	-0.8	2.2	0.17[a]

[a]: Z scores from Mann-Whitney Test
Abbreviations:
SD: standard deviation; IQR: interquartile range.
Mean diff: mean difference; ROM: Range of motion; Vmean: mean velocity; Vpeaks: mean of peaks velocity; NVP: number of velocity peaks; JPE: joint position error.

Compared to the control group, results from the independent t-test showed that patients with acute WAD presented with a significantly lower maximal cervical ROM in all movement directions ($p<0.001$). For those with acute WAD, their neck ROM was approximately 37% less in flexion, 43% less in extension, 27% less in right rotation, and 39% less in left rotation, compared to the ROM of the healthy participants.

Similarly, significant differences between groups were also observed for the mean and peak velocity where participants with acute WAD moved their neck slower than the healthy participants in all directions ($p<0.001$). Mean and peak velocity in the sagittal plane (neck flexion and extension) was slower than in the transverse plane of movement (neck rotation). Those with acute WAD had, on average, 30% of the mean velocity of healthy participants during active flexion and extension, compared to 32% in right and left rotation.

The NVP was significantly higher in those with acute WAD in all directions ($p< 0.001$), indicating that those with acute neck pain move their neck with more irregular movement. The movements with highest NVP were extension (mean difference 42.3) and flexion (mean difference 34.8), followed by left rotation (mean difference 34.4) and right rotation (mean difference 30.3).

Finally, head repositioning acuity measured as the JPE on return to neutral following active cervical rotation was not significantly different between groups in either right (mean difference 0.2; $p=0.39$) or left rotations (mean difference 0.7; $p=0.17$).

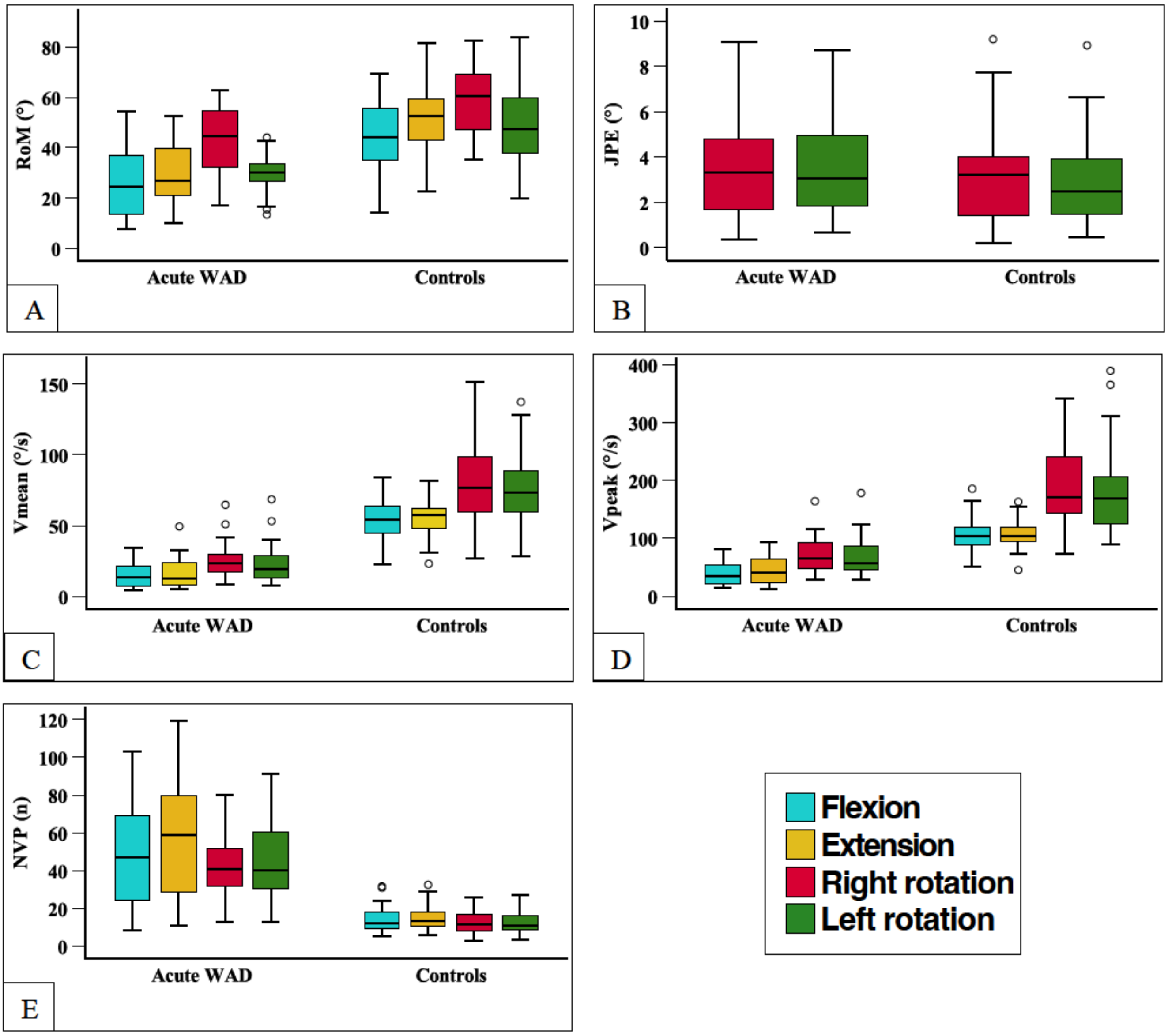

Figure 2.2: Box plots illustrate the features of cervical kinematics, including (A) range of motion (ROM), (B) joint position error (JPE), (C) mean velocity (Vmean), (D) peak velocity (Vpeak), and (E) number of velocity peaks (NVP).

2.4.2 Correlation between subjective reports and cervical kinematics

Table 2.3 presents correlations between self-reported outcome variables and kinematic measures in those with acute WAD. NDI was the self-reported measure that showed the greatest number of significant associations with kinematic measures (12 out of 18) (all p values < 0.05).

NDI was significantly correlated with mean velocity of movement in all directions (coefficients range from -0.48 to -0.62), with peak velocity in flexion, extension, and right rotations (r range= -0.44 to -0.70), with NVP in flexion, extension, and right rotations (r range= 0.42 to 0.45), and with cervical ROM in extension and right rotation (r range= -0.46 to -0.66). In contrast, the level of fear of movement measured via the TSK was not correlated with any of the kinematic measures. Recovery expectations largely did not correlate with the measures of cervical kinematics whereas the degree of catastrophising did correlate with the peak and mean velocity in flexion and extension as well as the ROM of extension.

Table 2.3: Correlation results between self-reported measures and neck kinematic measures of patients with acute WAD

Kinematic Measures	NRS [lower, Upper 95% CI]	NRS-ROM [lower, Upper 95% CI]	NDI [lower, Upper 95% CI]	TSK [lower, Upper 95% CI]	PCS [lower, Upper 95% CI]	Recovery Expectations [lower, Upper 95% CI]
Flexion						
ROM (°)	**-0.53*** **[-0.8, -0.08]**	**-0.52*** **[-0.79, -0.07]**	-0.33 [-0.69, 0.16]	-0.06 [-0.51, 0.42]	-0.36 [-0.71, 0.13]	0.13 [-0.36, 0.56]
Vmean (°/s)	-0.35 [-0.72, 0.17]	-0.37 [-0.73, 0.16]	**-0.62**** **[-0.86, -0.19]**	-0.26 [-0.67, 0.27]	**-0.46*** **[-0.78, 0.05]**	0.05 [-0.46, 0.53]
Vpeak (°/s)[a]	**-0.45*** **[-0.75, 0.08]**	**-0.43*** **[-0.74, 0.09]**	**-0.70**** **[-0.86, -0.23]**	-0.22 [-0.68, 0.22]	**-0.52*** **[-0.82, -0.11]**	0.06 [-0.39, 0.56]
NVP (n)[a]	0.09 [-0.5, 0.46]	0.05 [-0.44, 0.52]	**0.44*** **[-0.11, 0.73]**	0.37 [-0.09, 0.74]	0.13 [-0.36, 0.58]	0.11 [-0.45, 0.51]
Extension						
ROM (°)	**-0.60**** **[-0.83, -0.18]**	**-0.50*** **[-0.78, -0.04]**	**-0.66**** **[-0.86, -0.28]**	-0.25 [-0.64, 0.25]	**-0.68**** **[-0.87, -0.31]**	0.21 [-0.29, 0.62]
Vmean (°/s)[a]	-0.33 [-0.69, 0.2]	-0.32 [-0.67, 0.23]	**-0.58**** **[-0.82, -0.11]**	-0.36 [-0.79, -0.03]	**-0.43*** **[-0.8, -0.04]**	0.07 [-0.39, 0.56]
Vpeak (°/s)	-0.27 [-0.66, 0.24]	-0.26 [-0.66, 0.25]	**-0.55*** **[-0.81, -0.09]**	-0.36 [-0.72, 0.15]	**-0.53*** **[-0.8, -0.06]**	0.1 [-0.4, 0.55]
NVP (n)[a]	0.16 [-0.47, 0.52]	0.19 [-0.39, 0.59]	**0.45*** **[-0.13, 0.74]**	0.34 [-0.08, 0.77]	0.32 [-0.14, 0.74]	-0.05 [-0.58, 0.4]
Right Rotation						
ROM (°)	-0.39 [-0.73, 0.11]	-0.33 [-0.7, 0.18]	**-0.46*** **[-0.77, 0.02]**	0.05 [-0.44, 0.52]	-0.02 [-0.49, 0.47]	**-0.48*** **[-0.78, 0]**
Vmean (°/s)[a]	-0.23 [-0.6, 0.33]	-0.22 [-0.61, 0.33]	**-0.48*** **[-0.81, -0.07]**	0.02 [-0.67, 0.23]	-0.17 [-0.68, 0.22]	-0.14 [-0.44, 0.52]
Vpeak (°/s)[a]	-0.17 [-0.56, 0.39]	-0.11 [-0.54, 0.42]	**-0.44*** **[-0.76, 0.06]**	-0.13 [-0.67, 0.24]	-0.1 [-0.65, 0.26]	-0.23 [-0.44, 0.52]

(Continued)

Table 2.3: *(Continued)*

Kinematic Measures	NRS [lower, Upper 95% CI]	NRS-ROM [lower, Upper 95% CI]	NDI [lower, Upper 95% CI]	TSK [lower, Upper 95% CI]	PCS [lower, Upper 95% CI]	Recovery Expectations [lower, Upper 95% CI]
NVP (n)[a]	0.14 [-0.47, 0.49]	0.15 [-0.38, 0.57]	**0.42*** **[-0.08, 0.75]**	0.09 [-0.23, 0.67]	0.21 [-0.27, 0.65]	0.01 [-0.6, 0.34]
JPE (°)	-0.22 [-0.62, 0.28]	-0.17 [-0.59, 0.33]	-0.04 [-0.5, 0.43]	-0.22 [-0.62, 0.28]	0.24 [-0.25, 0.64]	**-0.53*** **[-0.8, -0.08]**
Left Rotation						
ROM (°)	-0.12 [-0.57, 0.39]	-0.04 [-0.51, 0.45]	-0.13 [-0.57, 0.37]	0.13 [-0.37, 0.58]	0.21 [-0.3, 0.63]	-0.21 [-0.63, 0.3]
Vmean (°/s)	-0.16 [-0.6, 0.34]	-0.18 [-0.61, 0.33]	**-0.52*** **[-0.8, -0.05]**	-0.31 [-0.69, 0.2]	-0.34 [-0.71, 0.17]	0.1 [-0.4, 0.55]
Vpeak (°/s)[a]	-0.26 [-0.64, 0.28]	-0.23 [-0.65, 0.26]	-0.38 [-0.78, 0.01]	0 [-0.64, 0.28]	-0.32 [-0.74, 0.09]	-0.03 [-0.36, 0.59]
NVP (n)	-0.09 [-0.55, 0.41]	0.1 [-0.4, 0.55]	0.32 [-0.19, 0.69]	0.29 [-0.22, 0.67]	0.23 [-0.28, 0.64]	-0.17 [-0.6, 0.33]
JPE (°)[a]	0.15 [-0.33, 0.59]	0.18 [-0.27, 0.63]	0.14 [-0.29, 0.61]	0.22 [-0.41, 0.52]	0.22 [-0.27, 0.63]	-0.2 [-0.71, 0.13]

Pearson product moment correlation coefficients (r) are presented, unless something else is specified: [a] Spearman's correlation. Significant correlation was indicated in bold (*P*<0.05 (*) or *P*< 0.001 (**)). NDI: neck disability index; NRS: numeric rating scale; NRS-ROM: neck pain taking immediately after neck motion tasks; PCS: pain catastrophising scale; Tampa Scale of Kinesiophobia; ROM: Range of motion; Vmean: mean velocity; Vpeaks: mean of peaks velocity; NVP: number of velocity peaks; JPE: joint position error; CI: confidence interval.

2.5 DISCUSSION

This study quantified cervical kinematic features in people with acute WAD and assessed their association with self-reported outcomes of pain, disability, catastrophising and fear of movement. In support of our hypothesis, the results demonstrate that people with a whiplash injury within the previous 15 days, present with restricted, slower and irregular movements in all directions compared to asymptomatic controls. Higher neck pain and disability in people with acute WAD is significantly associated with several kinematic features, including movement velocity and range. However, fear of movement was not associated with any of the cervical kinematic measurements. These findings suggest that pain and disability dictate changes in neck movement soon after injury, although causality can't be established at this stage.

2.5.1 Range of movement

This study found that maximal ROM was significantly lower in all directions in patients with acute WAD compared to asymptomatic controls. This finding is consistent with previous studies which reported restricted ROM in patients with acute (Fernández-Pérez et al., 2012, Kasch et al., 2001c, Kumbhare et al., 2005, Sterling et al., 2004) and chronic (Woodhouse and Vasseljen, 2008a, Sjölander et al., 2008, Armstrong et al., 2005, Baydal-Bertomeu et al., 2011, Dall'Alba et al., 2001, Madeleine et al., 2004, Grip et al., 2007, Kaale et al., 2007, Klein et al., 2001, Ohberg et al., 2003, Pereira et al., 2008, Prushansky et al., 2006, Puglisi et al., 2004, Shahidi et al., 2012) WAD, despite methodological differences. This study also found that restricted ROM was associated with pain intensity and pain-related disability, as observed in another study (Fernández-Pérez et al., 2012). This could indicate that patients with higher pain and disability tend to move their neck less likely due to the intensity of their pain. Reduced neck motion could be interpreted as protective mechanism to minimize the potential damage to the neck in agreement with the pain-adaptation model (Lund et al., 1991).

2.5.2 Mean and peak velocity of neck movement

To our knowledge, there are no studies that have measured the velocity of movement in patients with acute WAD. In the current study, the average mean and peak velocity during neck flexion, extension, and rotations were lower in those acute WAD compared to the control group. We also observed that the mean velocity of neck movement was negatively associated with neck pain-related disability and this was the case for all movement directions, that is, the greater the pain-related disability, the slower the neck moves. Given the cross-sectional nature of our data, we cannot draw firm conclusions regarding a cause-effect relationship. Interestingly, studies have reported reduced velocity of neck movement in patients with chronic WAD (Vikne et al., 2013, Grip et al., 2008, Ohberg et al., 2003) and chronic idiopathic neck pain (Sjölander et al., 2008, Tsang et al., 2013, Bahat et al., 2010, Röijezon et al., 2010). In comparison to individuals with chronic WAD, people with acute WAD moved their neck slower in all directions than those with chronic pain. For example, in this study, the average velocity of movement was 15.7 and 17.6 (°/s) during the acute phase compared to 27.6, and 23.6 (°/s) in patients with chronic WAD when performing neck flexion and extension, respectively (Vikne et al., 2013). Therefore, it would be relevant to investigate whether early signs of slow neck movements are predictive of the transition to chronicity.

2.5.3 **Cervical joint position error**

The current study found no significant differences between groups with regards to cervical proprioception measured as the JPE. Several studies have evaluated JPE in patients with either acute (Sterling et al., 2003b) or chronic (Armstrong et al., 2005, Feipel et al., 2005, Grip et al., 2007, Heikkilä and Wenngren, 1998, Kristjansson et al., 2003, Sjölander et al., 2008, Treleaven et al., 2003, Woodhouse and Vasseljen, 2008b) WAD, yet with inconclusive results. Sterling et al. (2003b) assessed JPE in patients with acute WAD presenting with moderate/severe disability which is similar to the level of disability of the current sample (Sterling et al., 2003b). The study found that patients with acute WAD and higher disability presented with a larger error of 2.2° and 1° compared to the healthy controls following right (significant differences) and left rotations (non-significant differences), respectively. We suspect that the lack of significance in the current studies is due to methodological differences or the variability among participants. We did not account for the presence of dizziness in our study, however, given that people with chronic WAD presenting with dizziness tend to show greater deficits in sensorimotor control

(Treleaven, 2011), subgrouping by the presence or absence of dizziness should be considered in future studies in acute WAD.

2.5.4 Smoothness of neck movement

Patients with acute WAD moved their neck with a high NVP in all directions which indicates that their movements were interrupted frequently and were not as smooth as that observed in asymptomatic controls. Previous work has shown that people with CNP either from traumatic or non-traumatic causes, display deficits in the smoothness of neck movement (Bahat et al., 2015a). While the underlying mechanism of irregular movement in patients with acute WAD remain unclear, other studies in patients with chronic WAD suggested that such a pattern might be a consequence of motor control disturbances (Grip et al., 2008, Sjölander et al., 2008). Therefore, the underlying mechanism of irregular movement soon after a whiplash injury should be investigated in further studies by measuring EMG in addition to cervical kinematics.

2.5.5 Association between self-reported measures and cervical kinematic features

A secondary aim of this study was to determine the relationship between self-reported measures and measures of cervical kinematic features in people with acute WAD. This study revealed that pain catastrophising is present soon after a whiplash injury. Findings from this study also indicated that the reduced velocity of movement and restricted motion during cervical extension were negatively associated with pain catastrophising. This interaction between the adapted motor behaviour (e.g. restricted motion and reduced velocity of movement) and catastrophising may feed into fear-avoidance model (Vlaeyen and Linton, 2000). It could be indicated that patients with acute WAD may restrict their cervical movement and slow down their motion as a protective and guarding mechanism to avoid excessive force and loading, hence decreasing neck pain. This notion is supported by a study conducted in people with LBP, where a negative association between the velocity of trunk movement and pain catastrophising was established (Vaisy et al., 2015). However, in the current study fear of movement was not associated with cervical kinematic features. One potential explanation for this could be the large variation in TSK scores among our participants with acute WAD with scores ranging from the lowest possible score (11) to the highest (44) on the TSK scale. In contrast, kinesiophobia, assessed via the TSK, was significantly associated with cervical kinematic features (ROM, velocity, and smoothness of movement) in people with CNP of traumatic and non-traumatic origin (Bahat et al., 2014a). These findings were also confirmed in people with chronic and RNP, where higher fear of movement was associated with altered quality of movement (Devecchi et al., 2022). It may be that during the acute phase, neck movement is more influenced by pain rather than fear or other psychological features. Notably, the NDI was the self-reported measure that showed the greatest number of significant associations with kinematic measures (12 out of 18).

One explanation for the strong association between neck disability and cervical kinematics is that neck disability provides a more comprehensive and objective picture of the impact of neck pain on an individual's overall functioning. Specifically, the NDI is a multidimensional measure that consists of 10 items related to pain intensity, personal care, lifting, reading, headaches, concentration, work, driving, sleeping, and recreation (Vernon and Mior, 1991). Altered cervical kinematics (i.e., restarted, slower, and irregular neck movement) may hinder the individual's ability to perform physical activities and carry out daily tasks, which could explain why altered movement was significantly correlated with neck disability. However, it's important to note that this is a speculation, and further investigation may be needed to determine the exact reason for the observed associations between features of cervical kinematics and neck disability.

2.5.6 Methodological considerations

A limitation of this study is the relatively small sample size of those with acute WAD which might reduce the generalisability of study findings. A pilot study to estimate the sample size was not conducted. Therefore, the findings from this study should be treated with caution due to the small number of observations. However, despite this, we were able to determine significant differences between groups for all cervical kinematics, apart for cervical proprioception. Additionally, a post-hoc power analysis (GPower 3.1.9.6, Kiel University, Germany) indicated that the current sample size and the observed effect size of 1.14 for the main outcome (neck flexion ROM) yielded a power of 98% at an alpha level of 0.05, supporting the sample size of the study. A further limitation in this study is that pre-existing conditions (e.g. pre-existing pain, restricted mobility) in patients with acute WAD prior to their inception were not considered. Nevertheless, these preliminary results prompt future longitudinal studies to evaluate the potential prognostic role that cervical kinematic measures may have in the transition from acute to chronic WAD.

2.5.7 Clinical implications

The current study indicated that patients with acute WAD moved their neck with slower and more irregular movement in all directions. These findings are also evident in people with CNP, either of traumatic or non-traumatic origin (Bahat et al., 2015b, Bahat et al., 2010, Gregori et al., 2008). Rehabilitation programmes typically focus on improving neck ROM, and there has been little emphasis on addressing other kinematic features such as reduced movement velocity, control, or quality of movement (Jull, 2011).

Evidence from people with CNP showed significant improvement in NDI, ROM, and velocity of movement following kinematic training (Bahat et al., 2015b). This earlier study investigated the effectiveness of cervical kinematic training on individuals with CNP who were randomly assigned to two groups (Bahat et al., 2015b). The first group performed kinematic training (KT) guided by a laser mounted on the head and performed active neck movements, quick head movements, static head positioning while moving the body, and smooth head movements following a target. The other group performed the same kinematic training but using a virtual reality device. The interventions consisted of 4-6 kinematic training sessions spread out over a 5-week period. The study showed significant improvement in NDI, ROM, and velocity of movement following kinematic training for both groups, and the effects were sustained for up to three months post-intervention (Bahat et al., 2015b). One potential explanation for such improvement in pain and disability is the improvement in the individual's capacity to move the head further, faster, and more precisely (Bahat et al., 2015b). It could be inferred that such an intervention could also be helpful for people with acute WAD. Thus, future studies should evaluate the value of kinematic training in the acute stage to enhance the velocity and smoothness of neck movements. Given that these features are associated with higher levels of pain and disability, addressing movement dysfunction may help to alleviate pain and even minimise the transition to chronicity. Although, longitudinal studies are required to corroborate this statement.

Our study found a significant negative association between the velocity of neck movement and neck pain-related disability. This may indicate that moving the neck faster may provoke the pain. Kinematic training with a VR device, as previously used (Bahat et al., 2015b), may be used to reduce neck pain associated with performing at a faster speed. This might be achieved using a VR device, as an intervention can be personalised for each participant based on their performance and pain tolerance.

2.6 CONCLUSION

In this chapter, findings indicate that people with acute WAD present with restricted, slower, and irregular neck movements. Most of the changes in neck movement were associated with higher neck pain intensity and disability, but not fear of movement. It is of clinical importance to assess whether these baseline measures are associated with persistent pain and disability following a whiplash injury. Based on the findings presented in this chapter, the next chapter explores whether the predictive ability of cervical kinematic features in individuals with WAD has been investigated before.

CHAPTER 3

IS PHYSICAL FUNCTION OF THE NECK REGION ASSOCIATED WITH POOR PROGNOSIS FOLLOWING A WHIPLASH TRAUMA?: A SYSTEMATIC REVIEW

The protocol for this systematic review has been published by the thesis author (Alalawi et al., 2019). This chapter reports in full the contents of a published manuscript by the thesis author (Alalawi et al., 2022d). It includes verbatim text from the published manuscript and some changes employed for the purpose of this thesis to allow greater justification of methodological choices.

Publications and Presentations

1. **Alalawi, A.**, Gallina, A., Sterling, M. and Falla, D., 2019. Are physical factors associated with poor prognosis following a whiplash trauma?: a protocol for a systematic review and data synthesis. *BMJ open*, *9*(11), p.e033298. **(Appendix 1)**

2. **Alalawi, A.**, Mazahari, M., Gallina, A., Sterling, M. and Falla, D., 2021. Are physical factors associated with poor prognosis following a whiplash trauma?: A systematic review. Physiotherapy UK 2020 Conference, Virtual.

3. **Alalawi, A**., Mazaheri, M., Gallina, A., Luque-Suarez, A., Sterling, M. and Falla, D., 2022d. Are Measures of Physical Function of the Neck Region Associated With Poor Prognosis Following a Whiplash Trauma?: A Systematic Review. *The Clinical journal of pain*, *38*(3), pp.208-221. **(Appendix 5)**

3.1 ABSTRACT

The predictive ability of cervical ROM was investigated previously in many reviews, but very few systematic reviews have examined the predictive ability of other physical features on poor outcome following a whiplash injury. This includes features related to subjective and objective measures (motor and muscular behaviour) of physical function. Therefore, the aim of this review was to synthesise the current evidence regarding the predictive ability of physical function in the prognosis of individuals following a whiplash injury.

In this systematic review, electronic databases were searched by two independent reviewers up to July 2020, including MEDLINE, EMBASE, CINAHL, PsycINFO, Scopus and Web of Science as well as grey literature. Eligible studies were selected by two reviewers who then extracted and assessed the quality of evidence. Observational cohort studies were included if they involved participants with acute WAD, followed for at least 3 months post-injury, and included objective measures or self-reported measures of physical function as prognostic factors. Data were not feasible for pooling and were synthesized qualitatively.

Fourteen studies (thirteen cohorts) were included in this review. Low to very low quality of evidence indicated that initial higher pain and disability and higher WAD grade were associated with poor outcome, while there was inconclusive evidence that neck ROM, JPE, activity of the superficial neck muscles, muscle strength/endurance, and perceived functional capacity are not predictive of outcome. The predictive ability of more contemporary measures of physical function such as neck movement velocity, smoothness of movement, variability of neck motion, and co-activation of neck muscles have not been assessed.

Although initial higher pain and disability and higher WAD grade are associated with poor outcome, there is little evidence available investigating the roles of physical function on prognosis following a whiplash injury.

3.2 INTRODUCTION

As discussed previously in Chapter One, section, 1.3.7.3 page 30, there is a high transition rate from acute to chronic WAD (Kamper et al., 2008, Hendriks et al., 2005, Carroll et al., 2008b) and, therefore, reducing this transition to chronicity is a priority. Chapter Two demonstrated that features of cervical kinematic are impaired in all directions shortly after a whiplash injury, with the majority of them associated with neck disability. Since such features were associated with the disability soon after injury, they could have the predictive ability to predict poor outcomes in people with WAD. Early identification of factors associated with developing persistent symptoms in WAD (Jull et al., 2011) is important as they could be targeted in a rehabilitation programme that may lower the transition to chronicity.

People with WAD are known to present with objective changes in physical function in the neck (Baydal-Bertomeu et al., 2011, Vikne et al., 2013). This includes increased activation of the superficial neck flexors (Sterling et al., 2003b), reduced maximum angular velocity of neck movements (Baydal-Bertomeu et al., 2011, Vikne et al., 2013) and reduced smoothness of neck movement (Vikne et al., 2013), as reviewed in Chapter One, Sections 1.3.2, 1.3.3, and 1.3.4. Moreover, other changes such as increased repositioning error (Mazaheri et al., 2021), reduced conjunct motion (Woodhouse and Vasseljen, 2008b), and changes in deep neck muscle activation (Schomacher et al., 2012) have also been observed in patients with chronic WAD. Of relevance, studies in acute WAD have revealed early changes in motor behaviour (Sterling et al., 2003b) which persist even after the acute phase (Sterling et al., 2003b, Schomacher et al., 2012) suggesting that these factors could play a role in the transition to chronicity.

Several systematic reviews have aimed to identify prognostic factors associated with poor outcome following a whiplash injury (Li et al., 2013, Daenen et al., 2013, Spearing et al., 2012, Goldsmith et al., 2012, Walton et al., 2009, Williamson et al., 2008, Kamper et al., 2008, Williams et al., 2007, Scholten-Peeters et al., 2003, Cote et al., 2001, Shearer et al., 2020, Carroll et al., 2008b, Walton et al., 2013b). Initial high levels of pain and disability (Scholten-Peeters et al., 2003, Williams et al., 2007, Kamper et al., 2008, Walton et al., 2009, Carroll et al., 2008b) as well as initial higher intensity of neck pain (Williams et al., 2007, Kamper et al., 2008, Carroll et al., 2008b, Walton et al., 2013b) have been identified as consistent predictors of poor outcome. Yet very few systematic reviews have examined the predictive ability of physical features on poor outcome following a whiplash injury. Of those conducted, the features examined were mostly cervical ROM (Kamper et al., 2008, Scholten-Peeters et al., 2003, Williams et al., 2007, Daenen et al., 2013, Shearer et al., 2020). Also, the activity of the superficial neck muscles was also assessed, but this was only in one study by Daenen et al. (2013), a study that have a similar aim to the current review.

However, it has been seven years since the previous study by Daenen et al. (2013) and a new literature search is needed as new knowledge may have emerged. Moreover, other contemporary physical factors commonly described in WAD, such as quality of neck movement or the extent of muscle co-activation, have not been considered to date in any review.

Therefore, the aim of this review was to update and summarise the objective and subjective measures of physical function that have been used in prognostic research following a whiplash injury and to synthesise and assess the overall quality of evidence on the predictive ability of these factors on neck pain and disability in individuals following a whiplash injury.

3.3 MATERIALS AND METHODS

This review was planned according to the guidelines for conducting prognostic reviews (Moons et al., 2014), and reported according to the guidelines from Preferred Reporting Items for Systematic reviews and Meta-Analyses (PRISMA) 2020 statement (Page et al., 2021), the Cochrane Back Review Group guidelines (Furlan et al., 2009), and the Cochrane Handbook (Higgins, 2011). The protocol for this review was registered prospectively on PROSPERO (International Prospective Register of Systematic Reviews) (CRD42019122559) on the 05/08/2019 and was published in advance (Alalawi et al., 2019).

3.3.1 Eligibility criteria

The PECOT framework (P=population; E=exposure; C=comparator; O=outcome; T=Type of study) was utilised to inform the inclusion criteria of this review (Higgins, 2011). The comparator component was not considered in this review given the nature of the research objective.

3.3.1.1 ***Population***

Studies were required to include participants aged>16 years old with acute WAD (<6 weeks) due to a motor vehicle crash or sports injury and classified as grade I, II, or III on the QTF classification (Spitzer et al., 1995). Moreover, primary studies needed to include at least a 3-month follow-up.

3.3.2 Exposure

Due to the inconsistency in the definition of physical function in the field of WAD, physical function was included in this review if it involved a body function or structure in the neck that can be measured objectively, for example, JPE, onset and amplitude of muscle activation, range, quality and velocity of neck movement, neck muscle strength and endurance, neck muscle fatigue, and balance. We also included self-reported measures of physical functioning, among others, physical component of the 36-Item Short Form Survey (SF-36) (Trust, 1994) and the NDI (Vernon and Mior, 1991) were selected. Additionally, the QTF Classification of WAD was included since the neck ROM is considered within the grading.

3.3.3 Outcome

The primary outcome of interest was the NDI (Vernon and Mior, 1991) measured at least at a 3-month follow-up. Other validated outcomes such as pain intensity, psychological status, health-related quality of life, self-rated recovery, and functional recovery were considered as secondary outcomes.

3.3.4 Type of study

Primary studies were included if they had an observational design and if they were published in English.

3.3.4.1 ***Exclusion criteria***

Studies were excluded if they included patients with previous neck or shoulder surgery, previous cervical pain that warranted treatment from a health care practitioner, or combined participants with WAD with patients reporting other musculoskeletal injuries.

3.3.5 Search Strategy

Several electronic databases were searched from 1995 to July 2020 including Medline (OVID), EMBASE (OVID), Cumulative Index to Nursing and Allied Health Literature

(CINAHL), PsycINFO (OVID), Scopus, and Web of Science. In addition, potential studies were searched in grey literature through ZETOC database, complemented by hand search of reference lists of relevant published reviews (Li et al., 2013, Daenen et al., 2013, Spearing et al., 2012, Goldsmith et al., 2012, Walton et al., 2009, Williamson et al., 2008, Kamper et al., 2008, Williams et al., 2007, Scholten-Peeters et al., 2003, Cote et al., 2001, Shearer et al., 2020, Carroll et al., 2008b, Walton et al., 2013b). A complete search strategy example was provided in the published protocol (Alalawi et al., 2019).

3.3.6 **Study Selection**

Eligible studies were selected by two reviewers (AA, MM) who independently screened titles and abstracts of all retrieved studies against the pre-determined eligibility criteria after removing duplicates. Eligible full text studies were screened by the same reviewers and any disagreement between the reviewers in the study selection process was resolved by discussion. A third reviewer (DF) was available to mediate any disagreement in data extraction.

3.3.7 **Data extraction**

Both reviewers extracted the data from a small number of eligible studies (n=5) independently (Moons et al., 2014). Due to similarity of extracted data between the reviewers, the rest of the eligible studies were extracted by the first reviewer (AA) and then their accuracy was confirmed by a second reviewer (MM). A third reviewer (DF) was available to mediate any disagreement in data extraction.

3.3.8 **Data items**

Extracted data were authors and year of publication, study location, study setting, time since crash, sample size, demographic characteristics, interventions received, prognostic factors, outcomes of interest, length of follow-up, methods for statistical analysis and findings.

3.3.9 **Risk of Bias**

The Quality In Prognostic Studies (QUIPS) tool (Hayden et al., 2013) was used to evaluate the risk of bias of included studies (Appendix 16). Two steps of assessment were used to facilitate the decision. Initially, each of the six domains in the QUIPS tool (study participation, study attrition, prognostic factor measurement, outcome measurement, study confounding, statistical analysis and reporting) was judged either as low, moderate, or high risk of bias, based on the number of fulfilled items under each domain. The chosen rating was judged using equally spaced cut-offs of 0-33% (high), 34%-66% (moderate), and 67%-100% (low). For example, if five of the six items of the first QUIPS domain (study participation) were fulfilled and reported, this domain was rated as low risk of bias, as 83% of items for this domain were reported. Finally, to assess the overall study quality, we classified a study to have a low risk of bias if five of the domains were low and none had high risk, a moderate risk of bias if a maximum of two domains were judged as moderate risk and the others were low risk and a high risk of bias if any domain was judged as high risk or had more than three moderate domains (Tseli et al., 2019). The items under each domain were tailored to this review. Two reviewers (AA,MM) assessed the risk of bias of each study independently. Any disagreement between the assessors in the assessment of risk of bias was resolved by discussion. A third assessor (DF) was available if needed.

3.3.10 Quality of evidence

Using the modified GRADE framework (Group, 2012), the overall level of evidence for a prognostic factor across studies was assessed by considering six elements including the phase of investigation, study limitations, inconsistency, indirectness, imprecision, and publication bias (Huguet et al., 2013, Iorio et al., 2015). More emphasis was placed on the phase of investigation with phase II and III explanatory studies rated as high level of evidence (Huguet et al., 2013) and phase I explanatory studies rated as moderate level of evidence. Following this, the evidence was downgraded based on the GRADE criteria as described before (Huguet et al., 2013). *Study limitations* was downgraded if most evidence came from studies with moderate or high risk of bias. *Inconsistency* for a prognostic factor was downgraded if the association between the factor and an outcome showed a variation in the direction (from significant to non-significant) with no or minimal confidence interval overlap. Additionally, it was downgraded if a prognostic factor was only presented in one study. With regards to *indirectness*, this element was downgraded if several tools were detected to measure a prognostic physical factor. Population and relevant outcomes were not considered in judging this domain as they were specified in the inclusion criteria (Goldsmith et al., 2012). *Imprecision* was downgraded if studies were unpowered, the width of confidence interval appeared excessively wide, or fewer number of studies and/or participants. Finally, *publication bias* was downgraded for all prognostic factors in this review due to the small number of studies for each potential physical factor, and the presence of publication bias in prognostic research (Hemingway et al., 2009).

The level of evidence was assessed by two reviewers (AA,MM) and rated as high, moderate, low, or very low. Any disagreement between the assessors in using GRADE was resolved by discussion. A third assessor (DF) was available if needed.

3.3.11 Data synthesis and analysis

Even though combining quantitative data from included studies was planned in advance, a meta-analysis was not feasible along with the assessments of heterogeneity, subgroup analysis, sensitivity analysis, and reporting bias. Subsequently, a qualitative synthesis of the results was conducted.

Before conducting this review, a protocol was published in advance, detailing the planned assessment of heterogeneity among included studies (Alalawi et al., 2019). In summary, heterogeneity of the pooled estimate was planned to be assessed using the Q statistic and the I^2 test. Statistical heterogeneity was considered significant between studies if $p<0.1$, as this test has low power (Lau et al., 1997). Beside the Q statistic and to measure the magnitude of heterogeneity, the I^2 test was planned to be used which gives a score range from 0-100%, where scores from (0% - 30%), (31% – 50%), (51 % - 70%), and (71% – 100%) indicates low, moderate, considerable, and substantial heterogeneity, respectively (Higgins and Green, 2008). However, the assessment of heterogeneity in this study was not possible. This is because of the variety of outcome measures used among studies in this review, as summarised in the results section. Another issue was that the same outcome was reported differently between studies. For example, the outcome related to pain intensity was reported as a continuous outcome in one study (Gun et al., 2005), while it was classified into three groups in another study (Berglund et al., 2006).

3.3.12 Patients and public involvement

The focus of this research was developed following consultations with patients with WAD, however, they were not involved in the analysis of this systematic review.

As part of designing this systematic review, the author of this study delivered a presentation detailing this study to members of a Patient and Public Involvement (PPI) group at the University of Birmingham, Birmingham, UK. The group consisted of patients, carers, and members of the public who collectively provided feedback on the presented project. Specifically, the meeting was mainly to ensure that the study is relevant, meaningful, and responsive to the needs and priorities of patients who had experienced a whiplash injury.

3.4 RESULTS

3.4.1 Literature Search

A total number of 14 studies met the inclusion criteria and were included in our review. The search strategy and reasons for exclusion are outlined in the PRISMA follow chart in Figure 3.1.

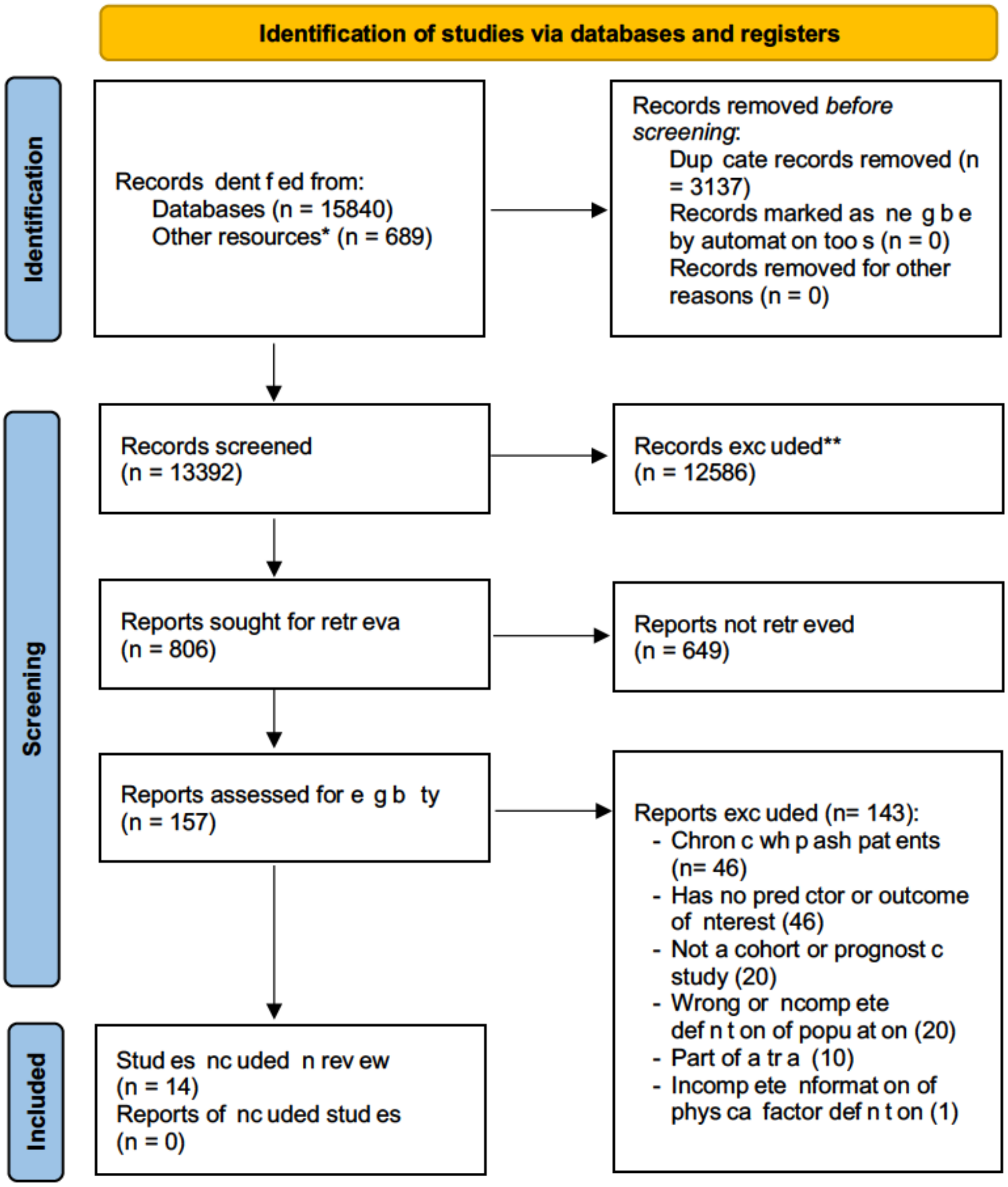

Figure 3.1: PRISMA 2020 flow diagram

3.4.2 Methodological quality

The methodological quality of each study is presented in Table 3.1. Five studies (Atherton et al., 2006, Kivioja et al., 2008, Berglund et al., 2006, Sterling et al., 2012, Ritchie et al., 2013) were assessed as having low risk of bias, four studies (Kyhlbäck et al., 2002, Sterling et al., 2006, Sterling et al., 2005, Hours et al., 2014) as moderate risk of bias, and five studies (Kasch et al., 2001b, Gun et al., 2005, Sterling, 2010b, Sterner et al., 2003, Hartling et al., 2001, Cobo et al., 2010) as high risk of bias. Studies that were assessed as moderate or high risk of bias were mainly due to limitations in the study attrition domain, not adjusting for important confounders, insufficient details for the statistical analysis and/or poor reporting.

Table 3.1: Risk of bias of included studies assessed using the QUIPS tool

Study	QUIPS Domains						Overall Risk of Bias
	Study participation	Study attrition	Prognostic factor measurement	Outcome measurement	Study confounding	Statistical analysis and reporting	
(Kasch et al., 2001b)	Low	High	Low	Moderate	Low	High	High
(Hartling et al., 2001)	Low	Moderate	Low	Moderate	High	Moderate	High
(Kyhlbäck et al., 2002)	Low	Moderate	Low	Low	Low	Moderate	Moderate
(Sterner et al., 2003)	Low	Moderate	Low	Moderate	Low	Moderate	High
(Gun et al., 2005)	Moderate	High	Low	Moderate	Low	Low	High
(Sterling et al., 2005)	Low	Moderate	Low	Low	Low	Moderate	Moderate
(Atherton et al., 2006)	Low	Moderate	Low	Low	Low	Low	Low
(Berglund et al., 2006)	Low	Low	Low	Low	Low	Moderate	Low
(Sterling et al., 2006)	Low	Moderate	Low	Low	Low	Moderate	Moderate
(Kivioja et al., 2008)	Low	Moderate	Low	Low	Low	Low	Low
(Cobo et al., 2010)	Low	High	Low	Low	High	Moderate	High
(Sterling et al., 2012)	Low	Moderate	Low	Low	Low	Low	Low
(Ritchie et al., 2013)	Low	Moderate	Low	Low	Low	Low	Low
(Hours et al., 2014)	Low	Moderate	Low	Moderate	Low	Low	Moderate

3.4.3 Description of included studies

All 14 included studies were cohort studies published between 2001 and 2014. Most of the included studies were conducted in Australia (Gun et al., 2005, Sterling, 2010b, Sterling et al., 2005, Sterling et al., 2006, Ritchie et al., 2013, Sterling et al., 2012) or Sweden (Kyhlbäck et al., 2002, Kivioja et al., 2008, Sterner et al., 2003, Berglund et al., 2006), with only one study from other countries including Denmark (Kasch et al., 2001b), UK (Atherton et al., 2006), Canada (Hartling et al., 2001) Spain (Cobo et al., 2010), and France (Hours et al., 2014) (Table 3.2). A description of the included studies is presented in Table 3.2 with additional details provided in Appendix 17.

The total number of participants included in the studies was 5954 (14 studies), with a sample size ranging from 76 to 2280 for single studies. Most participants were recruited from emergency departments while only one study included patients referred from an insurance company (Berglund et al., 2006). The average age of participants included in the studies ranged from 34 to 37 and the percentage of women ranged between 49% to 71%. Follow-up time ranged from 3 months to 3 years, with most studies investigating the prognostic ability of physical factors on outcomes at 6 and/or 12 months. The reported loss at follow-up ranged from 0% (Sterling et al., 2005) to 18% (Cobo et al., 2010) at six months and from 5% (Kivioja et al., 2008) to 41% (Berglund et al., 2006) at 12 months, with more information about loss of follow-up reported in Appendix 18.

Table 3.2: Description of included studies

References	Cohort No.	Country	Setting (number of sites)	Time from collision to inclusion in study	No. participants	Baseline age, mean (SD) (y)	Baseline sex (% female)	Intervention details
(Kasch et al., 2001b)	1	Denmark	Emergency Units (2)	1 wk	141	35.6 (10.7)	52.1	Participants received different interventions post injury Treatments included a soft cervical collar, physiotherapy treatment, chiropractic treatment, acetylsalicylic acid, NSAID, acetaminophen, opioids, and blockade
(Hartling et al., 2001)	2	Canada	Emergency department	Within the same day up to 48 h	380	37 (NR)	63.5	Received treatments include advice for using heat, use cold, use collar, neck exercise, rest, and medications
(Kyhlbäck et al., 2002)	3	Sweden	Orthopaedic clinic	Within 3 wk	83	35 (NR)	67	NR
(Sterner et al., 2003)	4	Sweden	Hospital emergency room and general practitioners	Within 1 mo	356	34.1 (12.1)	48.9	NR
(Gun et al., 2005)	5	Australia	Public hospital, medical and physiotherapy practices	Within 6 wk	147	35.6 (NR)	67	NR
(Sterling et al., 2005)	6	Australia	Hospital accident and emergency department, primary care practice, advertisement	Within 1 mo	76	36.27 (12.69)	71	Participants were allowed to pursue any form of treatment Several type of treatments and medications were reported including

(Continued)

Table 3.2: *(Continued)*

References	Cohort No.	Country	Setting (number of sites)	Time from collision to inclusion in study	No. participants	Baseline age, mean (SD) (y)	Baseline sex (% female)	Intervention details
								physiotherapy, chiropractic, acupuncture, simple analgesics, NSAIDS, codeine, anti-depressants, steroids, and opioids
(Atherton et al., 2006)	7	UK	Emergency department (4)	Median 8 d	765	Median (IQR): 34 (25-44)	56	NR
(Berglund et al., 2006)	8	Sweden	Insurance company	Within a few days	2280	36 (NR)	54	NR
(Sterling et al., 2006)	6	Australia	Hospital accident and emergency department, primary care practice, advertisement	Within 1 mo	76	36.27 (12.69)	71	Participants were allowed to pursue any form of treatment Due to recall bias, treatments received during the 18 mo period was not recorded
(Kivioja et al., 2008)	9	Sweden	Emergency	Within a wk	91	NR	54	Received treatments include analgesics medications, physical therapy and were encouraged to continue with normal activities
(Cobo et al., 2010)	10	Spain	Emergency unit	Within 1 mo	682	35.6 (13.5)	66.8	The patients were treated according to the established rehabilitation treatment protocol for neck pain after road traffic accident

(Continued)

Table 3.2: *(Continued)*

References	Cohort No.	Country	Setting (number of sites)	Time from collision to inclusion in study	No. participants	Baseline age, mean (SD) (y)	Baseline sex (% female)	Intervention details
(Sterling et al., 2012)	11	Australia, Canada, Iceland	Primary care practices, emergency departments, and through general advertisement	<3 wk duration	286	35.3 (13.08)	62.6	Physiotherapy was the most common form of treatment. Other treatments received included chiropractic, acupuncture, massage, simple analgesics, nonsteroidal anti-inflammatory drugs, opioid based medication, and adjuvant medications
(Ritchie et al., 2013)	12	Australia	Emergency departments, primary care practices, and via general advertisement	Within 1 mo	262	37.1 (14.2)	NR	NR
(Hours et al., 2014)	13	France	Emergency, secondary, and intensive care units	At time of accident	253	Reported as age groups from 16 to ≥ 55	68	NR

IQR indicates interquartile range; NR, not reported; NSAID, nonsteroidal anti-inflammatory drug.

3.4.4 Outcome measures

A variety of outcomes were used by eligible studies including outcomes related to pain and disability, pain severity, disability and return to work, and quality of life (Table 3.3).

Table 3.3: Summary of included physical prognostic factors and outcomes

References	Cohort No.	Prognostic Factor: Measurement, Instruments and Definition	Outcome: Measurement, Definition and Time Point	Length of Follow-up	Analysis	Findings
(Kasch et al., 2001b)	1	*Active cervical range of motion:* Neck flexion, extension, left/right lateral flexion, and left/right rotation measured using an inclinometer Dichotomized variable: total ROM of 2 SD below mean in control participants was considered as a risk factor *Neck flexion/extension submaximal (60%) workload:* Product of duration and load of an isometric endurance task for neck flexion/extension Dichotomize variable: workload of 2 SD below mean in control participants was considered as risk factor	*Disability and return to work:* Measurement tool: measured by a questionnaire composed of 6-item ranging from work capacity following injury to receiving pension due to injury Reduced working hours/ capacity, missing/ changing job, receiving job training, and receiving pension was regarded as handicap	6 and 12 mo	Cox regression analysis	Reduced active cervical ROM increased risk of handicap by a factor of *b*=2.5 (P<0.01) after 1 y, and by a factor of *b*=2.1 after 6 mo Neck muscle workload did not significantly predict long-term handicap at 1 y or 6 mo (P=0.39)
(Hartling et al., 2001)	2	*Quebec Classification of WAD (I-III):* Grade II of Quebec Classification was modified by subdividing patients into 2 groups: individuals with point tenderness and normal ROM and individuals with point tenderness and limited ROM	*Pain severity:* Measurement tool: measured by the severity and frequency of pain in the neck, shoulder, and/or upper back defined operationally as the presence of at least one of neck pain, upper back pain, or shoulder pain that met the predefined thresholds of intensity and frequency (≥3), provided by self-report	6, 12, 18, and 24 mo	Logistic regression analysis	WAD grade and presence of both tenderness and limited ROM were prognostic factors of presence of long-term symptoms

(Continued)

Table 3.3: *(Continued)*

References	Cohort No.	Prognostic Factor: Measurement, Instruments and Definition	Outcome: Measurement, Definition and Time Point	Length of Follow-up	Analysis	Findings
(Kyhlbäck et al., 2002)	3	*Quebec Classification of WAD:* Severity of initial injury measured using grade	*Pain-related disability:* Measurement tool: Pain Disability Index Was chosen to measure general and domain specific disability related to pain (0-70 points) Measured continuously with no dichotomization *Persistent neck pain:* Measurement tool: VAS Was used to assess pain intensity where the patients rated the pain experienced at the moment of survey Measured continuously with no dichotomization	3 and 12 mo	General linear model	WAD grade was not a significant predictor of pain-related disability at 3 or 12 mo WAD grade was a significant predictor of VAS at 12 mo follow-up
(Sterner et al., 2003)	4	*Quebec Classification of WAD:* Severity of initial injury measured using Quebec classification of WAD I, II, III	Disability and return to work interview: Disability related to the whiplash trauma Measured using a questionnaire that included items about the perceived effect of whiplash injury on daily living, leisure activities, and work situation Graded into 4 levels: none or minor; symptoms affecting work or leisure but not sick leave; change of work task; sick	16±2 mo after injury	Univariate and multivariate logistic regression analysis	WAD grades II-III was associated with poor prognosis

(Continued)

Table 3.3: *(Continued)*

References	Cohort No.	Prognostic Factor: Measurement, Instruments and Definition	Outcome: Measurement, Definition and Time Point	Length of Follow-up	Analysis	Findings
			leave due to the accident			
(Gun et al., 2005)	5	*Physical Component Scale of Short-Form 36 (SF-36)* *Questionnaire:* One subscale of SF-36 that measures the patient's own perception of his/her physical well-being Measured continuously	*Pain-related disability:* Measurement tool: Neck Pain Outcome Score (NPOS): The NPOS was obtained by modifying the Low Back Outcome Score questions by changing the focus of the questions from back pain to neck pain NPOS was structured so that an increase in score represents improvement Measured as a continuous outcome *Persistent neck pain:* Measurement tool: VAS Used to assess pain intensity VAS was structured so that an increase in score represents improvement Measured as a continuous outcome	12 mo	Linear and logistic regression	Physical Component Summary of SF-36 was not significantly associated with improvement in VAS after 12 mo follow-up
(Sterling et al., 2005)	6	*Active ROM*: Measured in 3 directions using an electromagnetic, motion-tracking device *Joint position error:* Defined as the participants' ability to relocate the head	*Pain-related disability:* Measurement tool: NDI Dichotomised at 6 mo postinjury to: Recovered (NDI< 8) Mild pain and disability (NDI 10-28)	6 mo	Linear and logistic regression	*Multivariate regression:* Initial NDI score and left rotation ROM were significant predictors of NDI at 6mo *Logistic regression:* Initial NDI score was significant predictor to

(Continued)

Table 3.3: *(Continued)*

References	Cohort No.	Prognostic Factor: Measurement, Instruments and Definition	Outcome: Measurement, Definition and Time Point	Length of Follow-up	Analysis	Findings
		to natural position following active cervical left and right rotation and extension Measured using an electromagnetic, motion tracking device *Superficial neck flexor muscle activity:* Surface electromyography was used to measure the activity of the sternocleidomastoid muscles during the craniocervical flexion (CCF) test *Pain-related disability:* Measured continuously	Moderate/severe pain and disability (NDI>30)			the group with persistent moderate/severe symptoms at 6 mo Initial NDI score and decreased range of cervical extension were significant predictors of membership to the group with persistent mild symptoms versus recovery at 6mo
(Atherton et al., 2006)	7	*Pain-related disability:* Dichotomize variable: NDI scores were categorized into tertials categorization of low, medium, and high *Quebec Classification of WAD:* From collected data, the severity of WAD was judged Severity of initial injury measured using grade Dichotomize variable: categorized into I, II, III classifications *Limitation of neck movement*	*Persistent neck pain:* Measurement tool: measured by VAS which was used to indicate the presence of pain in the neck area lasting for 1 d or longer in the week before questionnaire completion Persistent neck pain considered as the presence of pain in the post-collision and at each follow-up point (1, 3, 12 mo)	12 mo	Poisson regression	High scores of neck disability was significantly associated with persistent neck pain Grade II (1.2 [0.8-1.8]) and III (1.5 [0.7-3.4]) were not significantly associated with the persistent neck pain) compared with those with grade I injuries Limited ROM was not associated with persistent neck pain 0.9 (0.5-1.6)

(Continued)

Table 3.3: *(Continued)*

References	Cohort No.	Prognostic Factor: Measurement, Instruments and Definition	Outcome: Measurement, Definition and Time Point	Length of Follow-up	Analysis	Findings
		Measurement: information was gathered regarding the neck movement using a standard form Dichotomize variable: yes/no				
(Berglund et al., 2006)	8	*Subjective severity of whiplash injury by Quebec Classification of WAD:* Severity of initial injury measured using Quebec classification of WAD I, II, III	*Persistent neck pain:* Measurement tool: VAS (scale 0-100) VAS was treated a continuous and categorized into 3 groups: Low neck pain (0-30 VAS) Moderate neck pain (31- 54 VAS) Severe (55-100) *Pain-related disability:* Measurement tool: DRI The physical disability was assessed using the 12-item Was trichotomized and the cutoffs were the median (DRI=6) and the 75th centile (DRI=22) as measured on the baseline questionnaire	24 mo	Linear and logistic regression	Self-reported neck pain: Grade II and III were associated with having a higher neck pain intensity category at follow-up OR=1.5, OR=3.0, respectively Disability: A more severe whiplash injury was associated with having a higher degree of disability at follow-up
(Sterling et al., 2006)	6	*ROM:* Measured in the direction of flexion/extension and left/right rotation directions using an electromagnetic, motion tracking device Left rotation ROM was used in linear regression model, and cervical extension ROM was	*Pain-related disability:* Measurement tool: NDI Dichotomised at 2-3 y postinjury to: Recovered (NDI< 8) Mild pain-related disability (NDI 10-28) Moderate/severe pain-related disability (NDI>30)	2-3 y post-injury	Linear and logistic regression	*Linear regression:* Initial NDI scores predict poor NDI scores at 2 y. The previously significant prognostic factor left ROM rotation, was not significant predictor at 2-3 y *Logistic regression:* Initial NDI score was significant predictor to

(Continued)

Table 3.3: *(Continued)*

References	Cohort No.	Prognostic Factor: Measurement, Instruments and Definition	Outcome: Measurement, Definition and Time Point	Length of Follow-up	Analysis	Findings
		used in logistic regression model *Joint position error:* Defined as the participants' ability to relocate the head to neutral head position following active cervical left and right rotation and extension Measured using an electromagnetic, motion tracking device *Superficial neck flexor muscle activity:* Surface electromyography was used to measure the activity of the superficial neck muscles during the Craniocervical Flexion (CCF) test *Pain-related disability:* Measured continuously				the group with persistent moderate/severe symptoms at 2-3 y Initial NDI score was significant predictor of membership to the group with persistent mild symptoms versus recovery at 6mo The previously significant prognostic factor, cervical extension ROM, was not significant predictor at 2-3 y
(Kivioja et al., 2008)	9	*Quebec Classification of WAD:* Severity of initial injury measured using Quebec classification of WAD I, II, III	*Persistent neck pain:* Measurement tool: VAS (scale 0-100) Categorized into 2 groups: Severe neck pain (>30 VAS) Recovered (< 30 VAS)	1 y	Univariate and multivariate logistic regression	The WAD-classification did not predict persistent neck pain
(Cobo et al., 2010)	10	*Quebec Classification of WAD:* General description of the grades were given. The factor was dichotomized into WAD I and WAD II	*Persistent neck pain*: Measurement tool: VAS (scale 0-100) Measured at 6 mo postinjury and categorized into:	6 mo	Linear and multiple linear regression (stepwise method)	WAD grades were not related with poor recovery of VAS 6 mo after whiplash injury

(Continued)

Table 3.3: *(Continued)*

References	Cohort No.	Prognostic Factor: Measurement, Instruments and Definition	Outcome: Measurement, Definition and Time Point	Length of Follow-up	Analysis	Findings
			Mild pain 0-30 Moderate pain 31-59 Severe pain 60-100			
(Sterling et al., 2012)	11	*Pain-related disability:* Measurement tool: NDI used a continuous measure *Active ROM:* Measured using an electromagnetic, motion tracking device Only left rotation was included in the prediction model as it was a validation study for a previous model	*Pain-related disability:* Measurement tool: NDI Dichotomized at 12 mo postinjury to: Mild or no disability (NDI 0-28) Moderate to severe disability (NDI 30-100)	12 mo	Multivariate regression analysis	*Pain-related disability:* Initial scores of NDI were a significant predictor of poor outcomes 12 mo postinjury *Active ROM:* Neck left ROM was not a significant predictor of poor outcomes in NDI 12 mo postinjury
(Ritchie et al., 2013)	12	*Pain-related disability* Measurement tool: NDI *Active ROM:* Measured using an electromagnetic, motion tracking device Total neck rotation (sum of left and right neck rotation, flexion and extension) was included in the present study	*Pain-related disability* Measurement tool: NDI Dichotomised at 12mo postinjury to: Having developed chronic pain-related disability (NDI ≥ 30%) Partially/fully recovered (NDI <30%)	12 mo	Univariate and multivariate logistic regression (backward stepwise)	*Univariate:* Increased initial NDI and decreased initial ROM were significantly associated with increased odds of chronic moderate/ severe disability vs. recovered/milder disability *Multivariate:* Following a backwards stepwise multiple logistic regression, initial NDI, was significantly associated with moderate to severe disability
(Hours et al., 2014)	13	*Quebec Classification of WAD:* General description of the grades were given. The factor was dichotomised into WAD I and WAD II	*QOL:* Measurement tool: The World Health Organization Quality of Life tool (scale 0-100) QOL was expressed as dichotomous	12 mo	Linear and multiple Poisson regression	*QOL:* Grade I (OR= 1.17; CI: 0.79-1.74) and II (OR= 0.84; CI: 0.59-1.18) were not associated with poor QOL 12 mo postinjury

(Continued)

Table 3.3: *(Continued)*

References	Cohort No.	Prognostic Factor: Measurement, Instruments and Definition	Outcome: Measurement, Definition and Time Point	Length of Follow-up	Analysis	Findings
			variables: satisfactory vs. unsatisfactory QOL; and satisfactory vs. unsatisfactory with health status			

CI indicates confidence interval; DRI, Disability Rating Index; NDI, Neck Disability Index; OR, odds ratio; QOL, quality of life; ROM, range of motion; VAS, Visual Analog Scale; WAD, whiplash-associated disorder.

3.4.4.1 ***Pain and disability***

Pain and disability was assessed in seven studies (Sterling et al., 2006, Sterling et al., 2005, Kyhlbäck et al., 2002, Berglund et al., 2006, Gun et al., 2005, Sterling et al., 2012, Ritchie et al., 2013) that were reported for n=68 (1%) at a three-month follow-up (Kyhlbäck et al., 2002), n=76 (1%) at a six-month follow-up (Sterling et al., 2005), n=625 (11%) at a twelve-month follow-up (Kyhlbäck et al., 2002, Gun et al., 2005), n=1381 (23%) at a twenty-four-month follow-up (Berglund et al., 2006), and n=65 (1%) at two-three years follow-up (Sterling et al., 2006). Different measurement tools were used including NDI (Sterling et al., 2005, Sterling et al., 2006, Sterling et al., 2012, Ritchie et al., 2013), Neck Pain Outcome Score (NPOS) (modified from Low Back Outcome Score [LBOS]) (Gun et al., 2005), Pain Disability Index (PDI) (Kyhlbäck et al., 2002), and Disability Rating Index (DRI) (Berglund et al., 2006). A cut-off score of 30 in NDI was considered as poor outcome. Scores for PDI and NPOS were treated continuously with higher scores indicating poorer outcome for the former, and good outcomes for the latter. The definition of poor outcomes for DRI was defined as scores more than 75th centile (DRI=22) although this was not clearly stated in the study.

3.4.4.2 ***Pain intensity***

Neck pain outcome was assessed in seven studies (Atherton et al., 2006, Gun et al., 2005, Kyhlbäck et al., 2002, Kivioja et al., 2008, Berglund et al., 2006, Cobo et al., 2010, Hartling et al., 2001), that were reported for n=68 (1%) at a three-month follow-up (Kyhlbäck et al., 2002), n=891 (15%) at a six-month follow-up (Hartling et al., 2001, Cobo et al., 2010), n=1018 (17%) at a twelve-month follow-up (Atherton et al., 2006, Gun et al., 2005, Kyhlbäck et al., 2002, Kivioja et al., 2008, Hartling et al., 2001), n=176 (3%) at an eighteen-month follow-up (Hartling et al., 2001), and n=1507 (25%) at a twenty-four-month follow-up (Hartling et al., 2001, Berglund et al., 2006). Neck pain was measured using the 0-100mm Visual Analogue Score (VAS) (Atherton et al., 2006, Gun et al., 2005, Kyhlbäck et al., 2002, Kivioja et al., 2008, Berglund et al., 2006, Cobo et al., 2010), or a self-report of severity and frequency of pain in the neck, shoulder, and/or upper back (Hartling et al., 2001).

The definition of poor outcomes and the cut-off scores for previous scales were defined differently across the included studies. Atherton et al. (2006) defined persistent neck pain as pain that lasts one day or longer which is present at each follow-up period. Gun et al. 2005 used VAS to assess neck pain, but it was reversed so that an increase in score represented improvement (Gun et al., 2005). Kyhlbäck et al. (2002) assessed pain intensity using the VAS as a continuous outcome where the patients rated the pain experienced at the moment of completing the questionnaire. Besides defining outcomes continuously, other studies categorized the outcomes into good and poor outcomes. Kivioja et al. 2008 categorized the VAS into two groups, with recovered neck pain as <30 VAS on a 100mm scale and severe neck pain defined as >30 VAS

(Kivioja et al., 2008), whereas Berglund 2006 categorized VAS into low (0-30), moderate (31-54) and severe (55-100) (Berglund et al., 2006). Similarly, Cobo et al. 2010 categorized VAS into mild (0-30), moderate pain (31-59) and severe pain (60-100) (Cobo et al., 2010). Lastly, Hartling 2001 (Hartling et al., 2001) used a self-report questionnaire where poor outcomes were defined as pain in the neck, shoulder, and/or upper back that reached thresholds of intensity and frequency ≥3.

3.4.4.3 ***Disability and return to work***

Outcome related to disability and return to work was assessed in two cohorts (Kasch et al., 2001b, Sterner et al., 2003), that were assessed at 6 and 12 month follow-ups (Kasch et al., 2001b), and n = 296 (5%) at about sixteen-month follow-up (Sterner et al., 2003). This was measured using self-reported questionnaires that are related to handicap, disability, and work situation. Poor outcomes in these outcomes were categorised arbitrarily as described in Table 3.3.

3.4.4.4 ***Quality of Life***

Quality of life was assessed in one study (Hours et al., 2014), at a 12 month follow-up (n=171; 3%). It was measured using the World Health Organization Quality of Life tool which was dichotomised into satisfactory or unsatisfactory quality of life and health status.

3.4.5 **Prognostic factors (narrative synthesis)**

A total of seven baseline measures of physical function were synthesised qualitatively (Table 3.3).

3.4.5.1 ***Neck pain and disability***

The association between baseline NDI and outcomes (pain intensity and pain and disability) after a whiplash injury was assessed in five studies (Atherton et al., 2006, Sterling et al., 2006, Sterling et al., 2005, Sterling et al., 2012, Ritchie et al., 2013), including a total of 1389 (23%) participants. All studies (3 low, 2 moderate, 1 high risk of bias) indicated that initial high scores of NDI were significantly associated with poor outcomes in patients with acute WAD. This association was also confirmed in multivariate linear and logistic regression analysis where NDI remain associated with poor outcomes following injury (Sterling et al., 2006, Sterling et al., 2005, Ritchie et al., 2013).

3.4.5.2 ***Quebec Classification of WAD (Grade I-III)***

The association between initial WAD grade II and outcomes was assessed in seven studies (Atherton et al., 2006, Berglund et al., 2006, Hartling et al., 2001, Kivioja et al., 2008, Cobo et al., 2010, Kyhlbäck et al., 2002, Hours et al., 2014) including a total of 4534 (76%) participants. Five studies (2 low, 2 moderate, 1 high risk of bias) found that initial WAD grade II was not significantly associated with neck pain (Atherton et al., 2006, Kivioja et al., 2008, Cobo et al., 2010), neck pain and disability (Kyhlbäck et al., 2002) or quality of life (Hours et al., 2014) following a whiplash injury. However, three studies (1 low, 1 moderate, 1 high risk of bias) found that WAD grade II was significantly associated with higher scores of neck pain (Berglund et al., 2006, Kyhlbäck et al., 2002) and the presence of long-term symptoms (Hartling et al., 2001) following injury. This narrative analysis showed inconclusive evidence regarding the predictive ability of WAD grade II.

The association between baseline WAD grade III and outcomes was assessed in three studies (Atherton et al., 2006, Berglund et al., 2006, Kivioja et al., 2008) including a total of 3136

(60%) participants. With regards to initial WAD III, one study (low risk of bias) found that it was a significant predictor of higher pain scores (Berglund et al., 2006), while two studies (2 low risk of bias) found no significant association with pain intensity after a whiplash injury (Atherton et al., 2006, Kivioja et al., 2008). There was inconclusive evidence about the prognostic ability of WAD grade III.

The predictive ability of WAD grade I and a combination of WAD grade II and III were assessed in three studies (Cobo et al., 2010, Sterner et al., 2003, Hours et al., 2014) including a total of 935 (16%) and 356 (7%) participants, respectively. Cobo et al. (2010) (high risk of bias) and Hours et al. (2014) (moderate risk of bias) found that WAD grade I was not a predictor of poor outcome on pain intensity at six months and on quality of life at 12 months after the injury, respectively. Sterner et al. (2003) (high risk of bias) found that the combined WAD grades II and III were associated with poor outcomes with regards to disability and return to work.

3.4.5.3 ***Neck range of motion***

The association between baseline neck ROM and outcome was assessed in six studies (Kasch et al., 2001b, Atherton et al., 2006, Sterling et al., 2005, Sterling et al., 2006, Sterling et al., 2012, Ritchie et al., 2013) including a total of 1530 (26%) participants. Kasch et al. (2001b) (high risk of bias) found that reduced total active cervical ROM increased the risk of disability at 6 and 12 months. Decreased neck left rotation and extension at baseline were significantly associated with NDI six months following WAD (Sterling et al., 2005), and at 12 months when all neck movements were combined (Ritchie et al., 2013). These factors were no longer predictive of NDI when measured at 12 months (Sterling et al., 2012), after-2-3 years (Sterling et al., 2006), or when entered into multiple logistic regression (Ritchie et al., 2013). Atherton et al.

(2006) (low risk of bias) found that limited ROM (compared to no limited ROM) was not associated with persistent neck pain at a 12 month follow-up.

3.4.5.4 ***Joint position error***

N=76 (2%) were included in two studies (1 cohort) investigating the association between JPS error and NDI at six months (Sterling et al., 2005) and 2-3 years (Sterling et al., 2006). Both studies (both moderate risk of bias) found no significant association with poor outcomes at six months (Sterling et al., 2006) and 2-3 years (Sterling et al., 2005).

3.4.5.5 ***Superficial neck flexor muscle activity***

Two studies (1 cohort; both moderate risk of bias), with n=76 (2%), found that EMG activity of the superficial neck muscles was not a significant predictor of outcome at six months (Sterling et al., 2005) or at 2-3 years (Sterling et al., 2006).

3.4.5.6 ***Muscle strength/endurance***

One study (high risk of bias) (Kasch et al., 2001b), including n=141 (3%) participants, found that the ability of neck flexion/extension submaximal (60%) workload did not significantly predict long-term disability at six months or 12 months .

3.4.5.7 ***Functional status***

One study (high risk of bias) (Gun et al., 2005), including n=147 (2.8%) participants, found that higher scores in Physical Component Summary measure of SF-36 was not significantly associated with improvement in neck pain after 12 months follow-up (Gun et al., 2005).

3.4.6 Level of Evidence (GRADE)

A summary of quality of evidence of each physical factor in this review is presented in Table 3.4. The quality of evidence was downgraded from 'moderate' to 'very low' mostly due to issues concerning high risk of bias of included studies, inconsistency between effects and potential publication bias.

The GRADE analysis of NDI showed that there was evidence of low quality that baseline NDI was significantly predictive of poor outcome following a whiplash injury. Similarly, very low quality evidence existed for the predictive ability of combined grade II and III for poor outcomes in patients with WAD. Inconclusive evidence with very low quality was found for the predictive ability of initial neck range of movement, WAD grade II, and WAD grade III following acute whiplash injury. Evidence of very low quality found that factors related to JPE, neck flexor muscle activity, neck flexor muscle strength/endurance, functional status, and WAD grade I were not predictive of poor outcome.

Table 3.4: Summary of findings and overall quality as assessed with GRADE

Potential prognostic factor	Number of participants (% from the total)	Number of studies (cohorts)	GRADE elements Risk of bias	Inconsistency	Indirectness	Imprecision	Publication bias	Level of evidence
NDI	1389 (23%)	5 studies	✓	✓	✓	✓	✕	Low
Grade I	935 (16%)	2 studies	✕	✓	✓	✕	✕	Very Low
Grade II	4534 (76%)	7 studies	✓	✕	✓ **	✓	✕	Very Low
Grade III	3136 (60%)	3 studies	✓	✕	✓ **	✓	✕	Very Low
Grade II and III	356 (7%)	1 study	✕	✕	NA*	✓	✕	Very Low
JPE	76 (2%)	2 studies	✕	✕	✓	✓	✕	Very Low
Neck flexor muscle activity	76 (2%)	2 studies	✕	✕	✓	✓	✕	Very Low
Neck flexor muscle strength/endurance	141 (3%)	1 study	✕	✕	NA*	✓	✕	Very Low
Functional status	147 (3%)	1 study	✕	✕	NA*	✓	✕	Very Low
Neck ROM	1530 (26%)	6 studies	✓	✕	✕ ***	✓	✕	Very Low

GRADE: Grading of Recommendations Assessment, Development and Evaluation; NDI: Neck Disability Index; JPE: Joint position error; Range of motion
Phase: phase of investigation
For univariate and multivariate analysis: Significant: Studies with significant effect; Non- Significant: Studies with non-significant effect
For GRADE elements: ✓ no serious limitations; ✕ serious limitations
NA: Not applicable
For overall quality of evidence: High (++++), Moderate (+++), Low (++), Very Low (+).

*Only one study
** WAD grade collected from self-report and some from objective measures
*** Different methods for measuring neck ROM

3.5 DISCUSSION

This review synthesized the evidence about the prognostic ability of baseline measures of physical function in patients with acute WAD, based on 14 cohort studies including a total of 5954 participants. The key findings from this review confirmed that initial higher neck pain and disability and higher WAD grade are associated with poor outcomes, while there is inconclusive evidence that neck ROM, JPE, activity of the superficial neck muscles, muscle strength/endurance, and perceived functional capacity are not predictive of poor outcome. The level of evidence of most current findings was judged as very low as assessed by GRADE. Finally, this systematic review revealed that there were no primary studies that attempted to investigate the association between more contemporary measures of physical function such as neck velocity, smoothness of movement, variability of neck motion, and co-activation of neck muscles with poor outcome following a whiplash injury.

3.5.1 Pain related disability

This review found that initial higher scores of pain and disability measured by the NDI was a prognostic factor of poor outcome following a whiplash injury. This finding is consistent with previous reviews which reported that initial greater pain and disability predicted poor outcome following whiplash injury (Williams et al., 2007, Kamper et al., 2008, Carroll et al., 2008b, Walton et al., 2013b). Although the findings were consistent between reviews, the findings should be interpreted with caution due to the heterogeneity of the used outcomes and the wide variability in the cut-off values, as reported previously (Walton, 2009). Moreover, our review found the level of evidence of such association to be low, which means we have very little confidence in the estimate of such association.

3.5.2 Quebec classification of WAD (grade I-III)

Being graded with neck pain but with no physical signs (WAD grade I) following a whiplash injury did not show any predictive ability of poor outcome when compared to those with no complaints about neck pain (grade 0) (Cobo et al., 2010). One drawback for WAD grade I is that it does not measure the intensity of neck pain. Therefore, using Grade I solely for its prognostic ability may not provide useful clinical information.

Five studies found that WAD grade II (neck pain with physical signs) was not associated with poor outcome following whiplash injury (Atherton et al., 2006, Kivioja et al., 2008, Cobo et al., 2010, Kyhlbäck et al., 2002, Hours et al., 2014), while three studies (Berglund et al., 2006, Kyhlbäck et al., 2002, Hartling et al., 2001) found a significant association.

Inconclusive evidence was observed for WAD grade III compared to those with grade II. One study found that having neurological symptoms in addition to neck pain and physical signs, was a significant predictor of higher neck pain scores (Berglund et al., 2006), while two studies found no significant association with neck pain after whiplash injury (Atherton et al., 2006, Kivioja et al., 2008). Even though the estimated effects of these two studies were not significant (Atherton et al., 2006, Kivioja et al., 2008), the direction of estimation was in favour with an association of poor outcome. This was evident when these three studies were included in a meta-analysis by Walton et al. (2013b) who showed WAD grade III to be significantly associated with persistent neck pain 12 months post-injury. Moreover, the prognostic ability of WAD III was also confirmed in a recent systematic review (Shearer et al., 2020). It could be inferred that although we found inconsistency in the association between WAD grade III and poor outcomes, patients with physical and neurological symptoms post-injury may develop persistent poor outcomes more than those with no neurological deficits.

3.5.3 Neck range of motion

Our review found inconclusive evidence about whether reduced cervical motion is associated with poor outcome following whiplash injury. This finding is in line with previous reviews that found a limited association between restricted neck motion and persistent disability (Scholten-Peeters et al., 2003, Williams et al., 2007, Daenen et al., 2013), whereas no such association was found in another review (Kamper et al., 2008). One explanation for the different findings could be attributed to the different approaches used to measure and dichotomise neck motion by the included studies. For example, Kasch et al. (2001b) defined neck restriction as total ROM lower than 2 SD below mean in control subjects, Atherton et al. (2006) defined restricted neck motion as yes/no based on the patients' own perception, whereas Sterling et al. (2006) and Sterling et al. (2005) measured neck motion in each direction.

3.5.4 Joint position error and activity of the superficial neck muscles

Our review found that neck proprioception measured by JPE, EMG activity of the superficial neck flexor muscles during craniocervical flexion, and workload in neck flexors and extensors were not associated with poor outcome in patients with acute WAD. This is consistent with the findings that were reported from a previous review (Daenen et al., 2013). However, the previous findings were based on just one cohort for JPE and EMG activity (Sterling et al., 2006, Sterling et al., 2005), and one for muscle strength/endurance (Kasch et al., 2001b). It is evident that further studies are needed to investigate the predictive ability of muscle behaviour in patients following a whiplash injury.

Assessment of JPE has been reported in the literature for several other musculoskeletal conditions, including knee osteoarthritis, low back pain, and shoulder impingement syndrome.

Research has shown that individuals with knee osteoarthritis have increased JPE compared to healthy controls of a similar age (Felson et al., 2009). Similarly, individuals with LBP have been found to have higher JPE compared to healthy individuals, with the largest errors seen in the sagittal plane (Tong et al., 2017). Studies have also reported increased JPE in individuals with shoulder impingement syndrome compared to healthy individuals (Sahin et al., 2017). These findings suggest that JPE may be a common feature in various musculoskeletal conditions and may potentially play a role in the development and maintenance of these conditions.

The assessment of JPE in individuals with neck pain has several limitations that can affect its accuracy and reliability. For example, inter-rater reliability can be an issue as different raters may have different levels of accuracy and precision in their assessments (Juul et al., 2013). Furthermore, the type of instrument used for JPE assessment can also affect the results, as some instruments may be less reliable than others (de Vries et al., 2015). Pain and kinesiophobia can also influence an individual's ability to perform JPE assessments, making the results less accurate (Asiri et al., 2021). Kinesiophobia showed a moderately positive correlation with JPE in extension and rotation in people with neck pain (Asiri et al., 2021). Finally, age plays a significant role in how JPE worsens and increases as people age. According to one study, subjects who are older than 50 years old exhibit significantly higher cervical JPE (Alahmari et al., 2017).

3.5.5 **Functional status**

The SF-36 composes of eight different subscales of functional status including subscales related to Physical Functioning, Role Physical, Bodily Pain, General Health, Vitality, Social Functioning, Role Emotional and Mental Health (Trust, 1994). These subscales are combined into two scales named Physical Component Summary Score and Mental Component Summary Score (Trust, 1994). Our review found that Physical Component Summary of SF-36 was not significantly associated with a reduction of neck pain intensity after 12 months follow-up. Physical Component Summary of SF-36 was not reported in previous reviews but rather a complete overall score (Carroll et al., 2008b), Bodily Pain score (Williams et al., 2007), or Role Emotional score (Williams et al., 2007), which found to be associated with poor outcomes following whiplash injury. Given the limited evidence about the association between self-reported perceived physical functioning and outcomes in WAD, further studies are required.

3.5.6 **Strength and Limitations**

The current review has several strengths. First, the methodology of the current review, including the literature search, was thorough and rigorous following a previously published protocol. This resulted in 13 distinct cohorts compared to 3 cohorts in the study by Daenen et al. (2013) that investigated a similar aim to our review. Second, the current study utilized GRADE to assess the overall level of evidence, unlike the study by Daenen et al. (2013) which did not assess the level of evidence. Third, the list of excluded studies, with their reasons, are available for other researchers to use for future planning of a systematic review, which is are available in Appendix 19. Finally, the QUIPS risk of bias tool was tailored and provided in the article as a supplementary document to be used for prognostic studies in WAD population.

However, there are some limitations for this study. Despite our comprehensive search strategy, potential relevant prognostic studies might be possibly missed due to poor reporting and/or if they were published in a language other than English. Furthermore, the initial agreement on risk of bias ratings and criteria in this review varied between reviewers, an issue which was pointed out previously (Grooten et al., 2019). However, this risk was minimised by conducting multiple discussions sessions among the reviewers which resulted in tailoring the QUIPS criteria to this review. The calculation of agreement between assessors in risk of bias and GRADE framework was not planned *priori* for this review and therefore was not conducted.

3.6 CONCLUSIONS

This chapter is based on a systematic review which provided low to very low quality of evidence that higher pain and disability and higher WAD grade were associated with poor outcome following a whiplash injury. There was inconclusive evidence about the prognostic ability of factors such as neck movement, JPE, activity of the superficial neck muscles, muscle strength/endurance, and perceived functional status. More contemporary features such as neck movement velocity and smoothness of movement were not previously investigated and therefore further research in this area is required. Based on these findings of this chapter, the next chapter will explore the predictive ability of physical features related to neck movement and ongoing pain and disability six months following a whiplash trauma.

CHAPTER 4

CERVICAL KINEMATIC FEATURES AND CATASTROPHISING ARE ASSOCIATED WITH POOR RECOVERY FOLLOWING A WHIPLASH INJURY: PRELIMINARY FINDINGS FROM A LONGITUDINAL STUDY

The protocol for this chapter was published in advance (Alalawi et al., 2020), but the findings of this chapter have not been published yet. Major changes in the analysis of the data have been made compared to what it was planned in the published protocol. The context and the reason for this change in data analysis is fully reported in the methods section of this chapter.

Publications

1. **Alalawi, A.**, Luque-Suarez, A., Fernandez-Sanchez, M., Gallina, A., Evans, D. and Falla, D., 2020. Protocol: Do measures of physical function enhance the prediction of persistent pain and disability following a whiplash injury? Protocol for a prospective observational study in Spain. *BMJ Open*, *10*(10). **(Appendix 2)**

4.1 ABSTRACT

Features of cervical kinematics can differentiate between people with neck pain and healthy controls, but their predictive ability on poor outcomes has not been assessed in people with acute WAD. If proven to be relevant, a rehabilitation programme targeting altered kinematics could be employed, which may improve the outcomes and reduce the transition to chronicity in such individuals. The aim of this preliminary study was to investigate the association between cervical kinematic features collected at baseline and the presence of persistent pain and disability six months later in individuals with WAD.

In this preliminary study, data from participants with neck pain following a whiplash injury collected at baseline and at six months. All cervical kinematic features that were collected at baseline in Chapter Two were considered, including active cervical ROM, mean and peak velocity of movement, smoothness of movement, and proprioception. Furthermore, self-reported measures of neck pain, disability, catastrophising, kinesiophobia, and recovery expectations were also included. Descriptive statistics were used to present the demographics and values of NDI at six months. The associations between the outcome measure (NDI) at six months and baseline variables were investigated using Pearson's and Spearman's correlations.

The recruitment of participants in this study was severely disrupted because of the COVID-19 pandemic. As a result, only 18 participants were recruited and included in the analysis of this preliminary study, from the 150 participants that were initially planned. The mean NDI score was 12.1 ± 8.2 at six months. Correlation's analyses revealed that all baseline cervical kinematic features in extension were significantly associated with NDI at six months, with coefficients ranging from -0.42 to 0.47 ($p<0.05$). Further, pain catastrophising showed a significant correlation (r coefficients=0.59, $p=0.01$) with NDI six months after injury.

These preliminary data suggests that the cervical kinematic features examined in extension together with pain catastrophising were significantly associated with ongoing neck disability six months after a whiplash injury.

4.2 INTRODUCTION

The findings in Chapter Three indicated there are no previous studies have attempted to investigate the associations between contemporary features of cervical kinematics and ongoing pain and disability following whiplash injury. Measures of motor function have been limited to measures such as ROM (Sterling et al., 2003b, Dall'Alba et al., 2001, Kasch et al., 2001a, Kasch et al., 2008). Yet, other features of cervical movement may offer potential for improving prediction. For example, and as discussed in Chapter One, there is evidence describing changes in motor function in people with WAD (Baydal-Bertomeu et al., 2011, Sjölander et al., 2008). Decreased maximum angular velocity of neck movements has also been observed in individuals with chronic WAD when compared to healthy individuals (Baydal-Bertomeu et al., 2011). In addition, a significantly larger jerk index (measure of the smoothness of neck movement) has been reported in individuals with CNP of both insidious and traumatic onset, when compared to healthy individuals (Sjölander et al., 2008). In Chapter Two, we found that features of cervical kinematic can differentiate between people with neck pain and healthy control. Yet, the associations of these additional features with outcomes have not been investigated in individuals with acute WAD. The value of investigating the association between cervical kinematics and self-reported outcomes is that they are applicable in clinical practice. Moreover, a rehabilitation programme targeting altered kinematics could be employed, which may improve the outcomes and reduce the transition to chronicity.

To investigate this aim, a study was planned which is outlined in the published protocol (Alalawi et al., 2020). The study's purpose was to identify physical factors associated with the development of chronic pain and disability in a sample of 150 participants with a whiplash injury. However, the COVID-19 pandemic significantly disrupted the data collection, which resulted in a significantly lower sample size at the end of data collection. An alternative analysis of the data was necessary since this small sample size was not sufficient to power the initial study. Therefore, a preliminary analysis using correlation analysis was conducted as it can serve as an initial step to show which features are associated with the development of pain and disability. To our knowledge, no study has attempted to assess the associations between features of cervical kinematic and the extent of pain and disability six months later in individuals following a whiplash injury.

4.2.1 **Aims and hypothesis**

The aim of the current preliminary study was to investigate the association between cervical kinematic features collected at baseline and the presence of persistent pain and disability six months later in individuals with WAD. The study incorporated a wide variety of measures, including cervical kinematic measurements as well as self-reported pain, disability, and known psychological dimensions. In this preliminary analysis, we hypothesised that baseline measures of cervical kinematic and self-reported measurements would show correlations with the extent of pain and disability six months after whiplash injury.

4.2.2 Objective

- To investigate whether baseline measures of cervical kinematic features were associated with neck pain and disability in individuals with acute whiplash injury, six months post trauma.

4.3 MATERIALS AND METHODS

4.3.1 Design

The current study is the preliminary findings of a longitudinal analysis of patients with acute neck pain initiated following a whiplash injury. The current study involved the follow-up data of the individuals with acute whiplash who were previously included in Chapter Two.

Briefly, in Chapter Two, a convenient sample of 18 individuals with acute WAD were recruited from a single private physiotherapy clinic in Malaga, Spain. Details about the reasons for including participants from a physiotherapy clinic in Malaga, Spain, and not from Birmingham, UK, were reported previously in Chapter Two, section 2.3.1, page 40. The assessments were conducted independently by a designated physiotherapist who works at the clinic, with no involvement from the author of this thesis (AA). Participants were included in the study if they involved in a recent (previous 15 days) motor vehicle crash. Further details about the participants' eligibility criteria were reported in Chapter Two, section 2.3.3, page 42, with their baseline characteristics in Chapter Two, Table 2.1.

4.3.2 Deviation from the published protocol

The current study shows the preliminary findings that deviated from a pre-planned study. Before COVID-19, a study was planned a *priori* as per the published protocol (Alalawi et al., 2020). Briefly, in the protocol, we aimed to combine contemporary measures of physical function with psychological and pain-related predictive factors to uncover predictive factors linked to the development of persistent pain and impairment following a whiplash injury. A potential number of 150 participants were initially planned, and prognosis was supposed to be investigated using linear and logistic regression analyses. However, none of these were achieved.

The reason for not adhering to the protocol is that the sample size collected (n=18) was significantly lower than what it was initially planned, which did not power the planned analysis. This is the result of the COVID-19 lockdown as data collection had to be halted at the recruitment site (Malaga, Spain). Considering that the Ph.D. is a time-bound project and the fact that only data from 18 participants were available, an alternative analysis was needed. Therefore, the available data was analysed and presented as correlations between baseline measures and follow-up data, instead of regression analysis, with the aim of obtaining preliminary evidence to support the value of physical testing during the acute phase to support prognosis at a longer term follow up.

4.3.3 Kinematic measures and proprioception

Baseline measures including ROM, mean and peak velocity of movement, smoothness of movement, and proprioception were assessed in the current study. Furthermore, self-reported measures of neck pain, neck disability, kinesiophobia, catastrophising, and recovery expectations were included. Further details about these measures were reported previously in Chapter Two, section 2.3.7.1, pages 47-48, and are summarised in Table 4.1. All these objective and subjective measures were supposed to be included as candidate predictors to develop prognostic models, but this was changed to correlation analysis due to the small sample size.

Table 4.1: Summary of self-reported and physical measures that were included in the current study (adapted from the published protocol (Alalawi et al., 2020))

Domain/ measurements	Data collection instrument	Baseline commencing ≤ 15 days post-injury	Six months (Outcome assessment point)
Psychosocial features			
Catastrophising	PCS	✓	
Kinesiophobia	TSK	✓	
Recovery Expectation	NRS	✓	
Injury characteristics			
Disability	NDI	✓	✓
Pain characteristics			
Current neck pain intensity	NRS	✓	
Neck pain intensity at the end of neck range of motion tasks.		✓	
Physical measures			
Neck range of motion	G-Walk (flexion, extension, and rotations)	✓	
Neck angular velocity		✓	
Smoothness of Neck movement		✓	
Neck proprioception		✓	

PCS: pain catastrophising scale; TSK: Tampa Scale of Kinesiophobia; NRS: numeric rating scale; NDI: neck disability index

4.3.4 Outcome measures

NDI at six months following acute whiplash injury was the primary outcome selected to investigate its association with baseline measurements. The selection of outcome and time cut-off were selected a *priori* as per our published protocol (Alalawi et al., 2020). The results of NDI were interpreted using the established categorisation recovered (NDI<8), mild pain and disability

(NDI 10-28), and moderate/severe pain and disability (NDI>30) (Sterling et al., 2005). NDI scores were collected over the telephone at six months as specified in the protocol.

4.3.5 Statistical analysis

Descriptive summary statistics were performed on the participants' neck pain and disability at baseline and six months post injury. Furthermore, the association between baseline objective measures and self-reported outcome (NDI) at six months were assessed using Pearson's correlation or Spearman's correlation. The former statistical test was used when the data was normally distributed, while the latter was used when the data wasn't normally distributed as assessed by the Shapiro-Wilk Test. The strength of correlations was interpreted as little or no correlation (0-0.25), fair to moderate (0.26-0.50), moderate to good (0.51-0.75), or good to excellent (0.76-1) (Chiu et al., 2005). The included measurements at baseline are summarised in Table 4.1.

Of the 18 participants assessed at baseline, three participants (17%) were missing at six months. To handle missing values, multiple imputation was used to impute missing values in NDI (Sterne et al., 2009), with five imputations and 10 iterations per imputation. All analyses, including multiple imputation, were performed using SPSS 26.0 (IBM Corp., Armonk, NY, USA). A p value of <0.05 was considered statistically significant.

4.4 RESULTS

4.4.1 Characteristics of participants

Table 2.1 showed baseline characteristics of included participants with acute whiplash injury summarising their self-reported and physical measures.

From 18 participants included at baseline, 15 (83%) participants at six months completed the follow-up. Reasons for dropout as follow; one participant had not completed the six months follow-up without providing a reason for dropout. Another participant developed a stroke and was excluded from this study. One participant changed her phone number and could not be reached. However, all the data of the three missing participants was imputed.

Summary of follow-up questionnaires of neck pain and disability at baseline and six months is presented in Table 4.2. Participants with whiplash injury presented with a mild neck disability at six months, with mean values of 12.1 ± 8.2.

Table 4.2: Mean and SD values of NDI and NRS assessed at baseline and six months

Outcome	Mean ± SD (baseline) (n=18)	Mean ± SD (six months) (n=18)
NDI	32.8 ± 7.5	12.1 ± 8.2

NDI: Neck Disability Index
NRS: Numeric Rating Scale

4.4.2 Correlation between subjective reports and baseline cervical kinematic features

The correlation analysis between measures of ROM, peak velocity, mean velocity, and smoothness of movement (assessed by NVP) with self-reported outcome at six months is presented in Table 4.3.

Table 4.3: Correlations between baseline measures and neck disability assessed in acute WAD at baseline and six months

	NDI (baseline)		NDI (six months)	
Baseline	Pearson's r	*p*-value	Pearson's r	*p*-value
Flexion				
ROM (°)	-0.33 [-0.69, 0.16]	0.09	-0.19 [-0.6, 0.31]	0.23
Vmean (°/s)	**-0.62** [-0.86, -0.19]**	**0.005**	-0.4 [-0.78, 0.04]	0.05
Vpeak (°/s) [a]	**-0.70** [-0.86, -0.23]**	**0.001**	**-0.50* [-0.79, -0.02]**	**0.02**
NVP (n) [a]	**0.44* [-0.11, 0.73]**	**0.04**	0.31 [-0.17, 0.7]	0.12
Extension				
ROM (°)	**-0.66** [-0.86, -0.28]**	**0.001**	**-0.44* [-0.76, 0.02]**	**0.03**
Vmean (°/s) [a]	**-0.58** [-0.82, -0.11]**	**0.01**	**-0.48* [-0.76, 0.05]**	**0.03**
Vpeak (°/s)	**-0.55* [-0.81, -0.09]**	**0.01**	**-0.42* [-0.78, 0.01]**	**0.04**
NVP (n) [a]	**0.45* [-0.13, 0.74]**	**0.04**	**0.47* [-0.02, 0.79]**	**0.03**
Right Rotation				
ROM (°)	**-0.46* [-0.77, 0.02]**	**0.03**	-0.04 [-0.51, 0.45]	0.44
Vmean (°/s) [a]	**-0.48* [-0.81, -0.07]**	**0.03**	-0.11 [-0.56, 0.4]	0.34
Vpeak (°/s) [a]	**-0.44* [-0.76, 0.06]**	**0.04**	-0.04 [-0.5, 0.46]	0.44
NVP (n) [a]	**0.42* [-0.08, 0.75]**	**0.05**	0.26 [-0.33, 0.61]	0.17
JPE (°)	-0.04 [-0.5, 0.43]	0.43	0.1 [-0.4, 0.53]	0.36
Left Rotation				
ROM (°)	-0.13 [-0.57, 0.37]	0.31	0.3 [-0.22, 0.67]	0.12
Vmean (°/s)	**-0.52* [-0.8, -0.05]**	**0.02**	-0.09 [-0.58, 0.37]	0.36
Vpeak (°/s) [a]	-0.38 [-0.78, 0.01]	0.07	-0.16 [-0.59, 0.36]	0.29
NVP (n)	0.32 [-0.19, 0.69]	0.11	0.23 [-0.24, 0.67]	0.19
JPE (°) [a]	0.14 [-0.29, 0.61]	0.28	0.1 [-0.39, 0.54]	0.36
Questionnaires				
NRS	**0.66** [0.28, 0.86]**	**0.001**	0.28 [-0.26, 0.63]	0.14
NRS-ROM	**0.69** [0.33, 0.87]**	**<0.001**	0.35 [-0.18, 0.68]	0.08

(Continued)

Table 4.3: *(Continued)*

	NDI (baseline)		NDI (six months)	
Baseline	Pearson's r	*p*-value	Pearson's r	*p*-value
NDI	-	-	0.35 [-0.09, 0.73]	0.08
TSK [a]	0.32 [-0.22, 0.66]	0.10	0.04 [-0.2, 0.67]	0.43
PCS [a]	**0.41*** **[-0.06, 0.74]**	**0.05**	**0.59**** **[0.4, 0.89]**	**0.01**
Recovery expectations [a]	0.02 [-0.49, 0.44]	0.47	-0.16 [-0.52, 0.41]	0.28

Pearson product moment correlation coefficients (r) are presented, unless something else is specified: [a] Spearman's correlation. Significant correlation was indicated in bold ($P<0.05$ (∗) or $P< 0.01$ (∗∗)). ROM: Range of motion; Vmean: mean velocity; Vpeaks: mean of peaks velocity; NVP: number of velocity peaks; JPE: joint position error.

All measures of cervical kinematic features in extension were significantly associated with NDI at six months (coefficients ranged from 0.47 to -0.42). These associations are demonstrated in Figure 4.1 (A-D). Furthermore, peak velocity in flexion and PCS were significantly associated with NDI six months after the injury, which are demonstrated in Figure 4.1 (E-F).

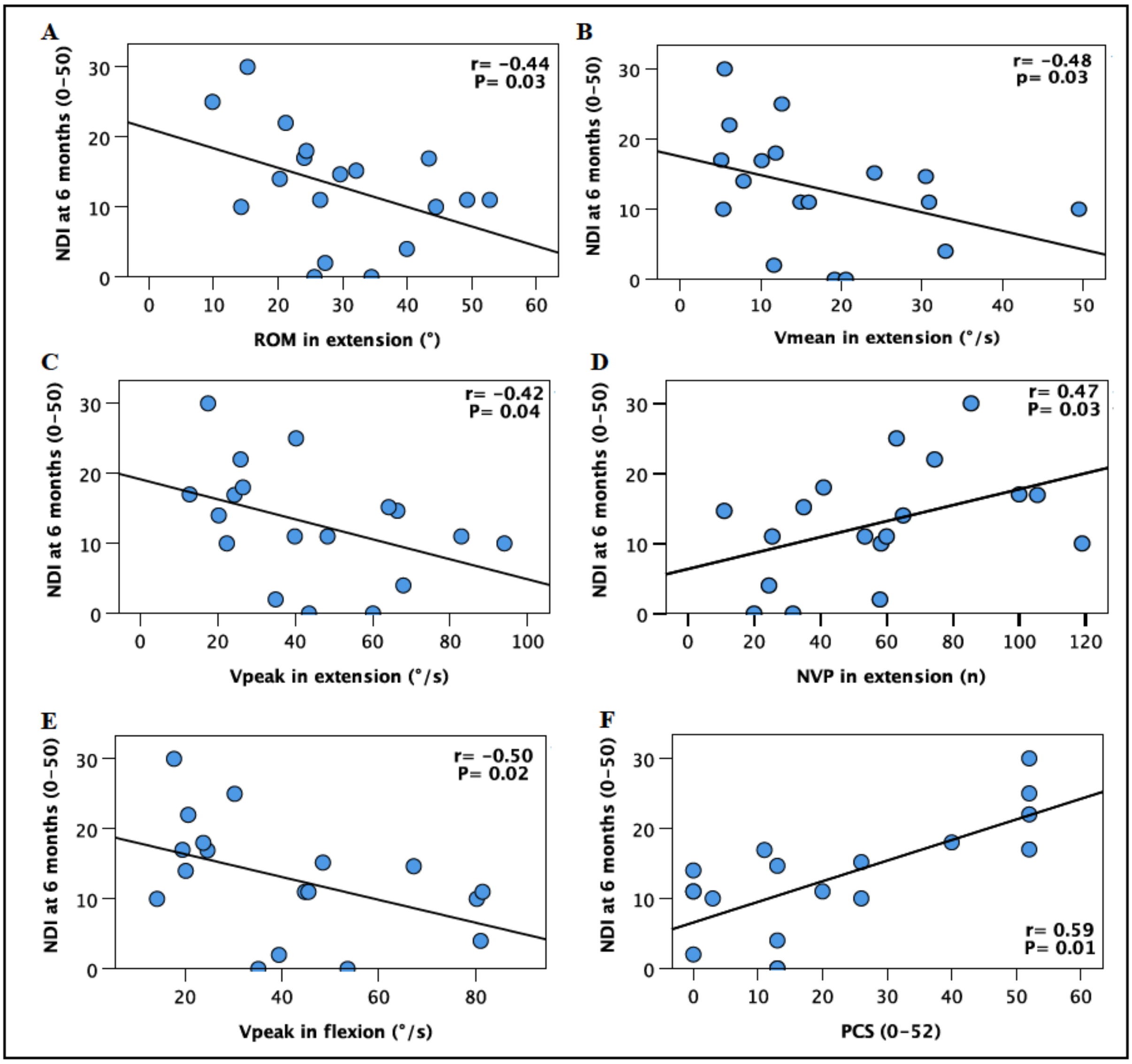

Figure 4.1: Results of the associations between neck disability index at six months and (A) range of motion in extension (B) mean velocity in extension (C) peak velocity in extension (D) number of velocity peaks in extension (E) peak velocity in flexion and (F) pain catastrophising scale

4.5 DISCUSSIONS

4.5.1 Summary of findings

This preliminary study investigated the association between cervical kinematic features collected at baseline and ongoing pain and disability six months following a whiplash trauma. All baseline objective (e.g. features of cervical kinematic) and subjective (e.g. self-reported measures) measurements were considered. The preliminary findings of the current study suggest that all ROM, velocity, and smoothness of movement during cervical extension may be associated with ongoing pain and disability six months after injury. Furthermore, the current preliminary study also suggests that higher pain catastrophising and slower cervical velocity in flexion were also associated with higher scores of neck pain and disability. These preliminary findings support our suggested hypothesis that various baseline measures of cervical movement and self-reported clinical measures may show associations with persistent neck pain and disability six months after a whiplash injury.

4.5.2 Association between features of cervical kinematic and neck disability

The current study suggests that restricted neck motion, slower velocity of movement, and jerkier movement during neck extension soon post whiplash trauma were associated with higher perceived disability at six months. Direct comparison with previous studies is not possible as this is the first study, but preliminary findings suggest that impaired motion characteristics in extension may play a higher role in the maintenance of neck pain and disability than flexion overtime.

The mechanism underlying the association between cervical kinematics in extension and poor outcomes six months later is not fully understood. Tissue injury during a whiplash injury is a common consequence of the sudden and forceful neck movements that occur during a whiplash event (Spitzer et al., 1995). As discussed in section 1.2.2, page 6, whiplash injuries can result in damage to the cervical facet joints, ligaments, and cervical muscles (Curatolo et al., 2011), with greater strains to the neck extensors (i.e., semispinalis capitis muscle) (Vasavada et al., 2007). An increasing body of research using in-vivo animal models of these tissues shows that when they are injured, several modifications can occur, including nociceptor activation, immediate and sustained dysfunction in afferents and spinal neurons, neuroplastic changes, and pain (Lee et al., 2008, Lee et al., 2004, Quinn et al., 2010). Hence, the presence of tissue damage in neck extensors may potentially explain why all cervical extension kinematic features were more strongly associated with perceived disability six months later.

4.5.3 **Association between pain catastrophising and neck disability**

The experience of higher pain catastrophising soon following whiplash injury may show association with higher neck pain and disability at six months in our sample. This finding is consistent with previous findings that found the same association of pain catastrophising (Walton, 2009). However, controversial evidence was found in a recent review by Luque-Suarez et al. (2020) summarising the role of pain catastrophising on neck pain and disability. The study found inconsistent, imprecise, and very low quality of evidence. The study (Luque-Suarez et al., 2020) found that greater level of pain catastrophising at baseline was associated with disability in three studies (Andersen et al., 2016, Bostick et al., 2013, Carstensen et al., 2012), whereas non-significant results were observed in two studies (Nieto et al., 2013, Kivioja et al., 2005).

Discrepancies in findings could be attributed to different levels of pain and disability. For example, these variables were associated with pain catastrophising in patients with WAD (Buitenhuis et al., 2008, Sullivan et al., 2002). Moreover, catastrophising is a dynamic attribute associated with certain constructs such as pain (Wade et al., 2012), although this was assessed following a knee arthroplasty. In our sample, individuals with WAD presented with higher average pain catastrophising than in other studies (Nieto et al., 2013).

4.5.4 Clinical implications

Findings from the current study suggest that impaired cervical kinematics during cervical extension at baseline can be associated with higher neck pain and disability six months post whiplash injury. Similarly, such an association was also reported previously in Chapter Two in individuals with acute neck pain following a whiplash injury. These findings stress the importance of assessing cervical kinematics soon after whiplash injury, which has been shown to be sensitive and specific in individuals with neck disorders (Bahat et al., 2015a). Furthermore, all identified features, including catastrophising, are potentially modifiable (Verwoerd et al., 2020), implying that strategies aimed at their alteration may aid in the prevention of chronicity. Further studies should consider investigating whether a rehabilitation programme that focuses on improving motion during cervical extension can improve outcomes overtime.

4.5.5 Strength and limitations

This is the first study to assess cervical kinematics within 15 days of a whiplash injury and followed them up to six months. However, this study has some limitations. The current sample of participants presented with a mild level of disability that was maintained throughout the six months study period. As a result, the generalizability of study findings is likely to be lower and may not be generalizable to those with higher disability. Moreover, the planned sample size published a *priori* in the protocol was not achieved (Alalawi et al., 2020), as data collection was severely distributed due to COVID-19. Subsequently, the pre-planned predictive analysis was not feasible to employ in this study. Instead, a simpler version of associations in terms of correlation analysis was adopted. Finally, a limitation to this study is that multiple testing of the correlation between baseline features and disability at six months could increase the risk of type I error. To reduce this risk, the Bonferroni correction could have been used in this study by adjusting the significance level to p=0.002 instead of p=0.05, based on the 24 features included in this study. However, this extremely low p-value could also increase the risk of a type II error. Therefore, the p-value was set at 0.05, a threshold that was used in a similar previous study with a similar sample size (Bahat et al., 2014a).

4.6 CONCLUSIONS

The preliminary findings of this chapter reveal that all features of cervical kinematic in extension, as well as pain catastrophising, were significantly associated with higher neck pain and disability six months after a whiplash injury. Findings in Chapter Two and Four indicated that features of cervical kinematic were altered in individuals with acute WAD with some of them associated with ongoing pain and disability six months following the injury. Further research should assess their presence and relevance with frequent episodes of pain in people with RNP during remission.

CHAPTER 5

ASSESSMENT OF MOVEMENT, NEUROMUSCULAR, AND PSYCHOLOGICAL FUNCTION IN PEOPLE WITH RECURRENT NECK PAIN DURING A PERIOD OF REMISSION: CROSS-SECTIONAL AND LONGITUDINAL ANALYSES

This chapter fully reports the contents of a published manuscript by the thesis author (Alalawi et al., 2022a). It includes verbatim text from the published manuscript and some changes employed for the purpose of this thesis to allow greater justification of methodological choices.

Publications and Presentations

1. **Alalawi, A.**, Devecchi, V., Gallina, A., Luque-Suarez, A. and Falla, D., 2021. Assessment of Neuromuscular and Psychological Features in People with Recurrent Neck Pain During a Period of Remission. IASP 21 Virtual World Congress on Pain. Virtual

2. **Alalawi, A.**, Devecchi, V., Gallina, A., Luque-Suarez, A. and Falla, D., 2022. Assessment of neuromuscular and psychological function in people with recurrent neck pain during a period of remission: Cross-sectional and longitudinal analyses. *Journal of clinical medicine*, *11*(7), p.2042. **(Appendix 3)**

5.1 ABSTRACT

Evidence suggests that even when pain subsides, some features of psychological and neuromuscular function might not always return to normal in people with neck pain. There is relatively little research exploring whether these adaptations exist in RNP patients who are pain-free. Additionally, it has not been investigated if these adaptations have the capacity to predict future recurrence of pain. The aim of this study was to examine for the presence of differences in neuromuscular and psychological function in individuals with RNP or CNP following a whiplash trauma compared to healthy controls. A secondary aim was to examine whether neuromuscular characteristics together with psychological features in people with RNP were predictive of future painful episodes.

This study is composed of two parts. The first is a cross-sectional observational study involving three groups of individuals: RNP, CNP, and healthy controls. The second part of this study involves a longitudinal analysis of people with RNP. Multiple features were assessed including neck disability, kinesiophobia, quality of life, cervical kinematics, proprioception, activity of superficial neck flexors, maximum neck flexion and extension strength, and perceived exertion.

Overall, those with RNP (n=22) and CNP (n=8) presented with higher neck disability, greater kinesiophobia, lower quality of life, slower and irregular neck movements, and less neck strength compared to controls (n=15). Prediction analysis in the RNP group revealed that a higher number of previous pain episodes within the last 12 months along with lower neck flexion strength were predictors of higher neck disability at a 6-month follow-up.

Participants with RNP presented with some degree of altered neuromuscular features and poorer psychological function with respect to healthy controls and these features were similar to

those with CNP. Neck flexor weakness was predictive of future neck disability. The results of this study highlight the importance of restoring neuromuscular function in individuals with RNP rather than only alleviation of their neck pain and perceived disability.

5.2 INTRODUCTION

Altered neuromuscular function is a common feature in patients with acute and CNP including those that have sustained a whiplash injury (Falla et al., 2004c, Falla et al., 2004d, Schomacher et al., 2012), which were discussed in Chapter One. Earlier work suggested that some measures of neuromuscular function may not always return to values seen in healthy people even when pain resolves (Jull et al., 2002, Sterling et al., 2001).

Findings from Chapter Three indicated that higher pain and disability post-injury in the acute phase, are the most consistent at predicting longer-term pain and disability (Alalawi et al., 2022d). However, the predictive ability of wide range of neuromuscular adaptations has not been conducted previously. Additionally, there is very limited evidence examining the presence of neuromuscular adaptations in patients with RNP, when they are pain free i.e., in a period of remission. A recent systematic review (Devecchi et al., 2021), aiming to determine whether neuromuscular adaptations exist in people with recurrent spinal pain found very low level evidence to support muscle activity changes in people with recurrent LBP, especially greater co-contraction, redistribution of muscle activity, and delayed postural control of deeper trunk muscles. Reduced ROM of the lumbar spine was also found. Meaningful conclusions on people with RNP could not be drawn since only one study was identified (Elsig et al., 2014). In that particular study, thirty people with recurrent episodes of neck pain of non-traumatic origin were included and neck proprioception and performance on the craniocervical flexion test (i.e., the maximum pressure maintained for 10 seconds) were examined (Elsig et al., 2014). Both measures were able to differentiate between people with RNP and healthy controls (area under the curve of 0.69 and 0.73 respectively). However, it should be noted that the participants with RNP were not entirely asymptomatic as they presented with mild neck pain (mean scores on NRS 3.13±2.01) and disability (mean scores on the NDI 10.7±5.12).

Currently there is very limited evidence on whether people with RNP who are in complete remission from their neck pain continue to display changes in cervical movement, neuromuscular function, or psychological features such as high levels of kinesiophobia which may impact on neuromuscular function. Additionally, the predictive ability of these features in people with RNP has not been previously investigated in people who have sustained a whiplash injury. Yet this is highly relevant since the identification of physical and psychological factors that may increase the risk of developing future episodes of neck pain would provide more specific direction for appropriate treatment for the prevention of repeated episodes of pain (Alalawi et al., 2019, Jull et al., 2011).

5.2.1 Aims and hypotheses

The aim of this chapter (aim 1) was to determine whether features of cervical kinematics, neuromuscular function, and selected psychological variables are altered in people with RNP following a whiplash injury when tested during a period of remission compared to healthy people and whether these factors are comparable between people with RNP and CNP. We hypothesised that people with RNP in pain remission would present with altered neuromuscular and psychological function similar to those present in people with CNP. The second aim (aim 2) was to investigate the predictive ability of a variety of neuromuscular and psychological features for the development of new pain episodes over 12 months in those with RNP. We hypothesised that a combination of neuromuscular and psychological features could predict future ongoing neck pain episodes over the 12 months of assessment.

5.2.2 Objectives

5.2.2.1 ***Aim 1 (cross-sectional analysis)***

1. To examine whether measures of cervical kinematic, neuromuscular, and psychological function are altered in participants with RNP during a period of remission compared to healthy controls.
2. To determine whether cervical kinematic, neuromuscular, and psychological function are comparable between participants with RNP during a period of remission and participants with CNP.

5.2.2.2 ***Aim 2 (longitudinal analysis)***

1. To identify features that predict future episodes of neck pain over 12 months in individuals with RNP following a whiplash injury.

5.3 MATERIALS AND METHODS

5.3.1 Study Design

A cross-sectional observational study followed by a longitudinal analysis for those with RNP, was conducted and is reported according to the guidelines of STROBE statement (Von Elm et al., 2014), with the STROBE checklist available in Appendix 20. The study was approved by the Ethical Review Committee of the University of Birmingham, UK (ERN_19-0564) and was conducted in accordance with the Declaration of Helsinki. Further amendments were also submitted with a summary of these amendments available in Appendix 21, with their ethical approval available in Appendix 22, Appendix 23, and Appendix 24.

5.3.2 Participants

Three groups of adult participants (≥ 18 years old) were included in this study consisting of people with RNP, CNP, and healthy controls. A sample size of 15 healthy controls (mean age ± SD:31.1±5.7; female: 60%), 22 participants with RNP (mean age ± SD: 31.0±11.8; female: 64%), and 8 participants with CNP (mean age ± SD: 33.6±8.7; female: 88%) were included in this study (Figure 5.1). Those with RNP and CNP had a history of neck pain initiated following a whiplash injury, due to a motor vehicle collision. Further inclusion criteria for each group are described below.

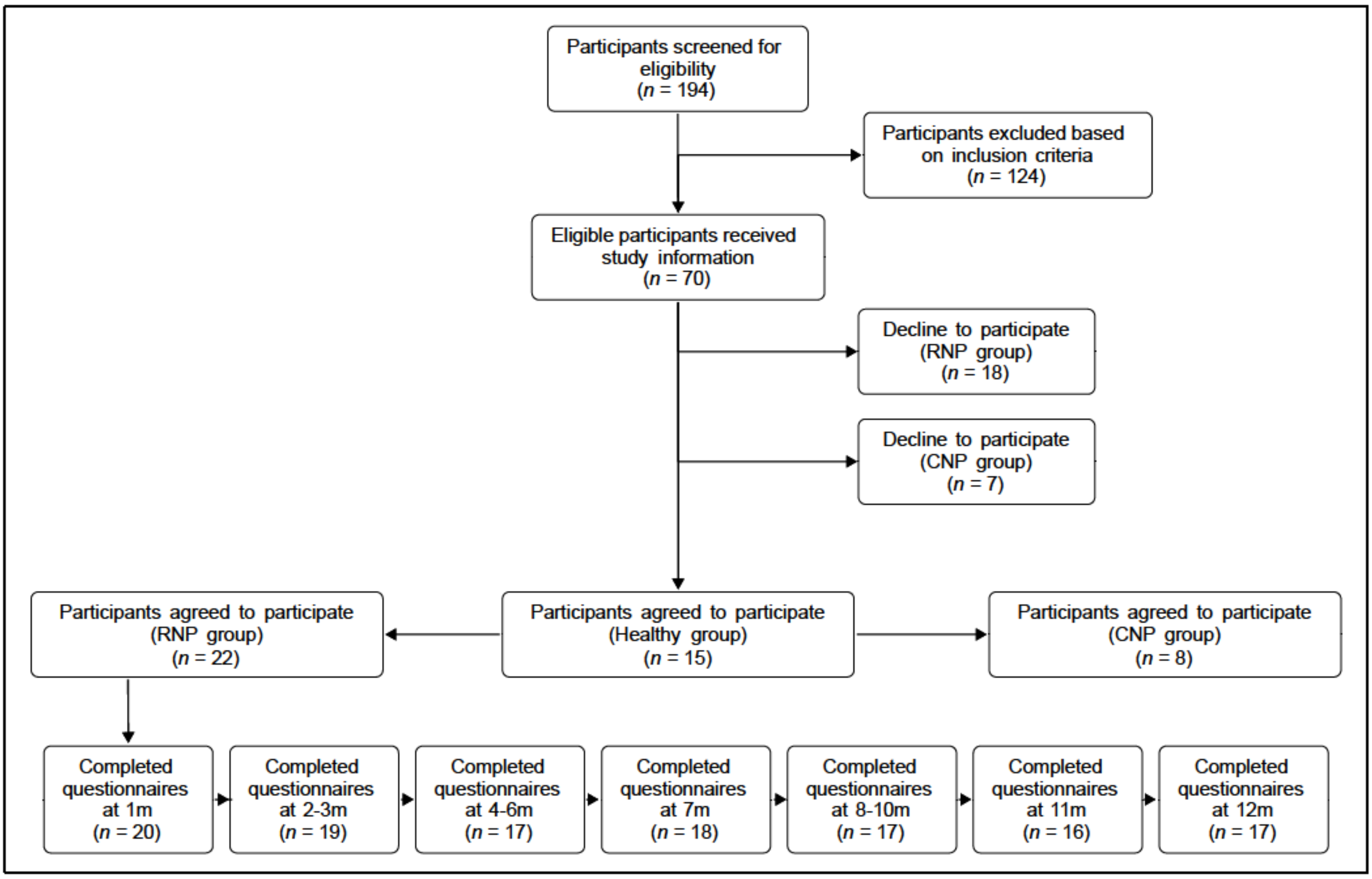

Figure 5.1: Flowchart of study population

*5.3.2.1 **RNP eligibility criteria***

Participants with RNP were included if they experienced two or more neck pain episodes (lasting ≥24 hours) separated by a period of remission lasting at least 30 days during the previous 12 months, and experienced neck pain of at least 2/10 on the NRS (Jensen et al., 1999) during an episode. These inclusion criteria are in line with the definition of recurrent LBP (Stanton et al., 2011). Furthermore, individuals with RNP needed to be pain free at the time of assessment.

*5.3.2.2 **CNP eligibility criteria***

Participants in this group were included if their neck pain lasted three months or more, and their current neck pain was at least 2/10 on NRS (Vernon and Mior, 1991).

*5.3.2.3 **Healthy participants eligibility criteria***

Healthy participants were required to have no current neck pain and no history of neck or shoulder pain that required treatment from a healthcare professional.

*5.3.2.4 **Exclusion criteria of all groups***

Participants were excluded if they participated in a neck or shoulder rehabilitation programme during the past three months or had any of the following: a history of neck or shoulder surgery (Crawford et al., 2004), malignant spinal disorders, rheumatic condition, mental disorders (Rosenfeld et al., 2000, Rosenfeld et al., 2003), pregnancy, or regular use of analgesic medication prior to the injury due to chronic pain.

5.3.3 Recruitment

All participants were recruited from the community in Birmingham, UK, including staff and students at the University of Birmingham. The study was advertised using posters, local newspaper, and social media (Facebook) to expand the reach of the study. Initially, a researcher (AA) assessed the eligibility criteria of potential participants, sent the participant information sheet to participants via email, and answered any questions via email or telephone. Once an interested and eligible participant was identified, they were invited to attend one session at the University of Birmingham where the study was explained, a hard copy of the information sheet was provided, and written informed consent was obtained. Once consent was obtained, all participants were asked to complete self-reported questionnaires and undergo physical testing which occurred on the same day. Participant's information sheet (Appendix 25, Appendix 26), study posters (Appendix 27, Appendix 28, Appendix 29, Appendix 30, Appendix 31), and informed consent (Appendix 32, Appendix 33) are included as Appendices. The data was collected by the author of this thesis (AA). Since both the recruitment and assessments of participants were conducted by the same assessor (AA), blinding was not possible.

5.3.4 Baseline measures (candidate predictors)

*5.3.4.1 **Patient-reported outcome measures***

The *number of episodes* referred to the number of pain episodes (over that last 12 months) that lasted more than 24 hours with at least 30 days remission. The *average pain intensity during an episode* was assessed using VAS (Langley and Sheppeard, 1985), ranging from zero (no pain) to 100 (worst pain imaginable). The validity and reliability of the VAS have previously been established (Boonstra et al., 2008, Breivik et al., 2000, Wainner et al., 2003). *Neck pain duration* was calculated in months and assessed only for the participants with CNP. *Current pain intensity* (for the CNP group only) was assessed using VAS immediately prior to physical data collection, by asking participants to indicate their current neck pain intensity.

To assess *perceived neck disability* at baseline, the NDI (Vernon and Mior, 1991) was used, with further details about this questionnaire are reported in Chapter Two, section 2.3.7.1, page 47.

The TSK was used to assess *fear of movement* or injury during activities (Roelofs et al., 2007). Further details about this questionnaire are reported in Chapter Two, section 2.3.7.1, page 47.

Health-related quality of life was quantified using the European Quality of life – Five Level (EQ-5D) that produces a single index value of range 0 to 1 where 1 is perfect health, and a VAS score ranging between 0–100, representing 'worst' to 'best' imaginable health state, respectively (Brooks, 1996). The EQ-5D, with each item having 5 possible responses, has improved inter-observer [ICC 2,1 0.57] and test-retest [ICC 2,1 0.69] reliability compared to the previous EQ-5D with three levels only (Janssen et al., 2008). The EQ-5D exhibits excellent psychometric characteristics across a wide variety of populations including musculoskeletal conditions (Feng et al., 2021).

Borg's scale (6-20) (Borg, 1998) was used to assess participants *perceived effort* performing submaximal contractions of their neck muscles.

5.3.5 Testing procedures

Prior to collecting physical data, all participants completed baseline self-reported outcomes (Table 5.1), with details provided in Appendix 34. All participants, including healthy controls, provided their demographics and completed measures of neck disability, kinesiophobia, and quality of life. Further questionnaires related to previous pain episodes and duration of neck pain were completed by individuals in the RNP group, and CNP group, respectively.

5.3.5.1 ***Cervical Kinematics and proprioception***

The procedures for collecting data related to features of cervical kinematic and proprioception was already reported in Chapter Two, section 2.3.6, page 45. The only difference is that the number of repetitions used in this chapter is 10 repetitions for assessing features of cervical kinematics. A greater degree of variability among participants with RNP and CNP was expected (Jull et al., 2018). Therefore, a large number of repetitions (10 repetitions) was selected, and this number was informed by previous studies involving people with neck pain (Alsultan et al., 2019) and healthy volunteers (Barbero et al., 2017).

5.3.5.2 ***Craniocervical flexion***

Tests of craniocervical flexion were performed involving two MVCs of CCF followed by four submaximal contractions (20%, 40%, 60%, 80, and 100% of MVC). To assess the MVC, craniocervical flexion strength testing was performed with the participant in supine lying with the hip and knees flexed to approximately 90 degrees (Falla et al., 2004d). The head was placed in neutral position and a dynamometer (NOD; OT Bioelettronica, Italy) was placed behind the upper cervical region with the instruction ‘to nod as if saying yes but as hard as you can, without lifting the head off the bed’. Each maximum MVCs lasted 3 seconds, separated by 1 minute rest in between repetitions (Lindstroem et al., 2012).

In the same position described for the MVC, participants were instructed to perform craniocervical flexion at 20%, 40%, 60%, and 80% of their maximal force, attempting to hold the force for 10 seconds at each level. Visual feedback on force displayed on a tablet was used to guide the participant to reach and maintain the target force for the duration of the contraction. During this task, the amplitude of SCM activity was measured with EMG.

Unlike Chapter Two, the activity of SCM was collected in this chapter, and that was because a different system to collect EMG activity was available for use in this study (details in section 5.3.6.3, page 131). Moreover, this study was conducted in a controlled laboratory setting at the university. The study in Chapter Two was conducted in a clinical setting where many factors, such as environmental artefacts, couldn't be controlled.

5.3.5.3 ***Maximal neck extension/flexion (isometric contractions)***

Two MVCs of both neck flexion and extension were performed using a Multi-Cervical Unit (MCU) (Hanover, MD, BTE Technologies); each MVC lasted 3 seconds with one minute rest in between. Participants were comfortably seated on the chair of the MCU with their hips and knees flexed to 90 degrees, their head in neutral position and feet flat on the MCU stand. To measure neck flexion strength, the load cell of the MCU was placed over the forehead and the participant was instructed to 'push as hard as you can as you try to bring your chin to your chest' (Pearson et al., 2009). Once two trials were completed, the load cell was then placed on the back of the head and the patient was instructed to 'push as hard as you can into the load cell as if trying to bring the back of the head to your neck' (Pearson et al., 2009).

Table 5.1: Summary of collected data across groups and their time point

Data collection point	Domain	Variables	RNP	CNP	Healthy controls
Baseline	Demographics	Age	✓	✓	✓
		Gender	✓	✓	✓
		Height	✓	✓	✓
		Weight	✓	✓	✓
	Patient-reported measures	NDI	✓	✓	✓
		TSK	✓	✓	✓
		EQ-5D	✓	✓	✓
	Others	Number of neck pain episodes	✓		
		Average of pain episodes (VAS)	✓		
		Neck pain duration		✓	

(Continued)

Table 5.1: *(Continued)*

Data collection point	Domain	Variables	RNP	CNP	Healthy controls
Baseline		Current pain intensity		✓	
	Objective measures	Cervical Kinematics (ROM, velocity, and smoothness)	✓	✓	✓
		Neck proprioception	✓	✓	✓
		Peak score of CCF	✓	✓	✓
		Muscle activity during submaximal CCF contractions	✓	✓	✓
		Maximum neck strength in flexion and extension (MVC flexion and Extension [kg])	✓	✓	✓
		Perceived exertion during the submaximal task in flexion and extension (Borg's scale)	✓	✓	✓
Outcome measures	Questionnaires	Number of days with pain	✓		
		NDI	✓		

RNP: Recurrent neck pain; CNP: chronic neck pain; CCF: Cranio-Cervical Flexion.

5.3.6 Instrumentation

5.3.6.1 *Inertial Measurement Unit*

Neck kinematic and proprioception assessments were collected using a wearable IMU (Research PRO IMU, Noraxon, USA), with a sampling rate of 100 Hz. The dimensions for the sensor are 37.6x52x18.1mm, and its mass is 34 grams. The two sensors were fixed over the participants' forehead and thoracic spine (T1) (Sjölander et al., 2008), using double-sided tape. The signal was acquired using the software myoRESEARCH 3.12 (Noraxon, USA). The reliability of measuring cervical movements with an IMU was established. A study was conducted to determine the test-retest reliability of the IMU over time by measuring the cervical ROM in healthy participants twice (Yoon et al., 2019). The study found fair to excellent reliability (ICC values ranged from 0.75 to 0.99) between the two measurements for all three anatomical directions (flexion-extension, axial rotation, and lateral bending). Furthermore, the study also found relatively small values for the standard error of measurement (SEM) (values ranged from 0.48° to 1.78°) and minimal detectable change (values ranged from 1.33° to 4.93°). A similar SEM (1.43° ± 0.42°) for this device was identified in another study when measurement error was assessed in healthy participants during the performance of different tasks of daily living (Mundt et al., 2019).

5.3.6.2 ***NOD dynamometer and Multi-Cervical Unit***

Isometric MVC during neck flexion and extension were measured using a MCU (BTE Technologies, Inc.™, Hanover, USA). Moreover, the MCU was used to assess isometric submaximal (25% of MVC) voluntary contractions during neck flexion and extension. The reliability of measuring cervical strength with the MCU has been established (ICC ranging from 0.92 to 0.99) in individuals with neck pain (Chiu and Lo, 2002). Additionally, CCF MVC and submaximal CCF contractions were measured using a NOD device (OT Bioeletronica, Italy), a hand-held dynamometer. The reliability of the NOD dynamometer was previously assessed during the performance of isometric neck flexion and extension (Mak, 2022). The study found good to excellent reliability between two assessors when assessing neck strength in flexion and extension (ICC values of 0.93 and 0.89, respectively). When reliability was assessed at different sessions, good reliability was found when assessing neck strength in flexion and extension (ICC values of 0.84 and 0.89, respectively). For validity, the agreement between the measurements of NOD and MCU was poor to good for neck flexion (Pearson correlation coefficient = 0.71), and good to excellent for extension (Pearson correlation coefficient = 0.95) (Mak, 2022).

5.3.6.3 ***EMG analysis***

Surface EMG (Ultium® EMG System, Noraxon, USA) was acquired from the SCM during the submaximal craniocervical flexion contractions.

The skin was first shaved, if needed, rubbed with gel (Nuprep, Weaver and Company) and then washed with water using cotton wool. Noraxon dual EMG wet gel electrodes (EMG electrodes, Noraxon, USA) were utilised which are disposable, wet-gel, self-adhesive Ag/AgCl snap electrodes. The electrode has a figure 8-shaped with an adhesive area of 40 mm x 22 mm, with dual circular electrodes of 10 mm diameter, and a fixed inter-electrode distance of 20 mm. Electrodes were placed 'over the distal one-third of the muscle (sternal head)' (Falla et al., 2002) for the SCM muscle.

Raw data was collected via the Ultium EMG sensor (Noraxon, USA) using the Noraxon MyoMuscle software (myoRESEARCH, Noraxon, USA) which was then transferred to Matlab (Mathworks Matlab 2019b) for processing. A band-pass filter of 20–400 Hz (order: 4) was used to process EMG signals (Park et al., 2013). The EMG signals were sampled at 2000 Hz and converted with a 16-bit A/D converter.

5.3.7 **Baseline objective measures (candidate predictors)**

All data were analysed in Matlab (Mathworks Matlab 2019b). Signals related to neck movement were low pass–filtered (cut-off frequency of 10Hz; order: 10) before computing the kinematic features. The start and end of the movement were defined as the time when the angular velocity exceeded a threshold of 5% of the peak velocity (Sjölander et al., 2008). Although some studies used a threshold of 10% of the peak velocity to determine the start and stop of movement (LoPresti et al., 2000, Michaelsen et al., 2001), using a threshold of 5% was deemed appropriate since we hypothesized that patients with RNP and CNP may present with lower peak velocity, therefore minimizing loss of data during the analysis.

Moreover, the choice of 5% threshold was tested on our data during the pilot study of this project and considered appropriated for retaining representative data.

Cervical ROM, mean velocity, peak velocity, and NVP were assessed during all directions with JPE was during cervical rotations. Further details about these measures are already reported in Chapter Two, section 2.3.7.2, page 48.

Maximum Cranio-Cervical Flexion Strength (CCF MVC [N]) refers to the highest score achieved following the two maximal isometric contractions. Muscle activity during submaximal CCF contractions refers to the normalized EMG amplitude achieved during each of the four levels of submaximal isometric contractions (20%, 40%, 60%, and 80% of CCF MVC force). A 1 second sliding window was used to estimate the amplitude as a Maximal Root Mean Square (RMS) (Falla et al., 2012). Two RMS values (for the right and left SCM) were obtained for each level of submaximal isometric contraction and these values were then normalized relative to the maximum EMG amplitude measured during the CCF MVC. The mean of both normalized values (right and left SCM) was included in the analysis (Jull and Falla, 2016).

Maximum neck strength in flexion and extension (MVC flexion and Extension [kg]) refers to the peak force achieved following the two repetitions of each maximal neck isometric contractions.

Perceived exertion during the submaximal task in flexion and extension (Borg's Flexion and Extension) refers to the value of perceived exertion assessed on the Borg's scale (6-20) (Borg, 1998) recorded immediately after completing the submaximal isometric contraction in flexion and extension at 25% MVC sustained for 30 seconds.

5.3.8 Outcome measures for the longitudinal analysis (prediction model)

Two outcome measures were used to evaluate the predictive ability of physical and psychological measures (Table 5.1) in patients with RNP following a whiplash injury. All outcomes were treated as continuous variables without dichotomisation. This approach follows the recommendations by PROGnosis RESearch Strategy (PROGRESS) series recommending the analysis of continuous variables on their continuous scale (Riley et al., 2013), and this method increases the statistical power and reduces information loss.

To collect the outcome measures in this study, for each month of a 12-month follow-up, participants were instructed to record their neck disability, number of days with neck pain, and the average pain intensity during the previous month, which are available in Appendix 35. These data were recorded each month using the electronic system Research Electronic Data Capture (REDCap) which enabled the researchers to monitor and manage the data collecting process via a web interface (Harris et al., 2019). The system provided an individualised link, involving the outcome measures, that was sent automatically each month for each participant.

5.3.8.1 ***Primary outcome***

The NDI score was selected as the primary outcome, which was assessed six months following baseline assessments. Using six months as a cut-off for identifying outcome was selected a priori (Alalawi et al., 2020, Sterling et al., 2010). NDI is widely used to evaluate perceived neck disability in people who have sustained a whiplash injury (Michaleff et al., 2014, Sterling et al., 2012), and is a reliable and valid outcome (Lemeunier et al., 2019).

5.3.8.2 ***Secondary outcome***

The secondary outcome was the number of days with pain. The mean number of days with pain over the course of 12 months was considered, unlike the primary outcome (NDI), which was only collected at 6 months. This outcome was defined as the number of days with neck pain during the previous month that lasted at least 24 hours, with pain intensity of at least 20/100 on a VAS. This was measured using the questions ‘Over the past month, how many days have you experienced neck pain?’ and ‘Over the past month, how would you rate your average neck pain intensity?’. The response for the first question is an absolute number, while a VAS score (0-100) was used to quantify pain intensity. The outcome and its definition have been used before in participants with LBP (da Silva et al., 2019), although pain intensity was assessed on a scale from 0-10. The selection of this outcome is of clinical importance as it captured pain that is relevant to the patients (Eklund et al., 2018). The mean number of days with pain per participant across the 12 month follow-up period was included in the analysis.

5.3.9 **Sample size**

A sample size of 50 participants with RNP, 15 with CNP, and 15 healthy controls was initially planned. These numbers were not achieved, except for the control group, due to the COVID-19 pandemic which severely disrupted data collection for this project.

5.3.10 **Statistical analyses**

5.3.10.1 ***Cross-sectional analysis***

Descriptive statistics were performed for participant demographics, and the data from self-reported questionnaires, cervical kinematic features, proprioception, and maximal and submaximal tasks. The normality of data distribution for self-reported and objective measures was assessed using the Shapiro-Wilk Test. If data was not normally distributed for the measure of interest ($p \leq 0.05$), differences among groups were assessed using the Kruskal–

Wallis test, after which the post-hoc test (Dunn's test) was performed for making multiple pairwise comparisons.

If data was normally distributed ($p \geq 0.05$) for a measure, the following steps were conducted. Initially, homogeneity of variance was assessed using Levene's test for equality of variances. If a feature was homogenous (Levene's test value: $p \geq 0.05$), results from one-way Analysis of Variance (ANOVA) was used. Two-way ANOVA was applied to evaluate the EMG amplitude during the performance of CCF, with group (RNP, CNP, and control) and submaximal force level (20%, 40%, 60%, 80% of MVC) as factors. When a feature was non- homogenous (Levene's test value: $p \leq 0.05$), results from Welch ANOVA was used. Finally, Tukey post hoc test was performed following one-way ANOVA and two-way ANOVA, while Games-Howell post hoc test was used following Welch ANOVA.

5.3.10.2 ***Longitudinal analysis***

To identify the predictive value of baseline measurements on NDI at six months and on future episodes with neck pain over 12 months period, a modelling approach of two-step was used (Alalawi et al., 2022b). Firstly, Least Absolute Shrinkage and Selection Operator (LASSO) regression was used to reduce the number of candidate predictors entering into second stage analysis. A cross-validation of 5-fold was used in this study considering the sample size, with further details about LASSO regression (Alalawi et al., 2020, Tibshirani, 1996, Pavlou et al., 2015) and cross-validation (Browne, 2000) reported elsewhere.

LASSO combines linear regression and variable selection (Tibshirani, 1996). It's a regularisation technique that reduces the magnitude of the coefficients of less significant features towards zero, which helps to address overfitting issues. As a result, the model completely excludes some features, producing a sparse model. LASSO is more effective at handling smaller datasets because it helps to reduce the model's variance, which can result in overfitting in smaller datasets (Pavlou et al., 2015). LASSO minimises the complexity of the model and can result in better generalisation performance by reducing the coefficients of less significant features towards zero (Tibshirani, 1996). By shrinking the coefficients of less important features towards zero, LASSO reduces the complexity of the model and can lead to improved generalisation performance.

LASSO regression was used in the current study as it is feasible for estimating models with multiple predictors in a small sample size (Jacobucci et al., 2019) and avoiding overfitting the data (Riley et al., 2019). The analysis was performed on all baseline candidate predictors reported in Table 5.1. Candidate predictors with no predictive power or those that were highly correlated were penalized and reduced to zero. This penalisation (shrinkage) approach is used to effectively exclude candidate predictors from the final model by shrinking their coefficients to exactly zero (Tibshirani, 1996). Candidate predictors with zero coefficients were excluded from entering stage two. The second step was to perform multivariate linear regression analysis on candidate predictors with regression coefficients of more than zero that were identified from LASSO (first stage). R statistical software was used to conduct this analysis. The functions, packages, and codes that were used to analyse this data have been described elsewhere (Liew et al., 2020a).

For this study, data from individuals with full cases for each model were considered. As a result, the observation number differs between models, as used previously (Puschmann et al., 2020). For example, 17 participants with complete data were considered to develop the model with NDI, while 19 were considered for the model involving the outcome of number of days with pain.

Multiple imputations to deal with missing data in this study was not conducted. This is because all missing data were in the dependent variables (outcomes). Also, according to a previous study, multiple imputation is unnecessary for analysing longitudinal data as findings showed that multiple imputation was highly unstable when the multiple imputations were repeated 100 times (Twisk et al., 2013).

The Mean Squared Error (RMSE) (Rüschendorf, 2014) was used to quantify the prognosis error between predicted and observed values in each generated prognostic model. This is a measure to assess the internal validity of a model (Wippert et al., 2017). RMSE is interpreted on the same scale of an outcome. For example, NDI scores range from 0 to 50, and therefore RMSE can range from 0 to 50 too.

5.4 RESULTS

5.4.1 Characteristics of participants

Demographic characteristics and results for the self-reported questionnaires at baseline are reported in Table 5.2. Mean age (SD) was 31.1±5.7 for the healthy participants, 31±11.8 for RNP, and 33.6±8.7 for those with CNP; the majority were females in all three groups. No significant differences were observed in participant demographics, except for height (p = 0.02). The mean score of average neck pain intensity for those with RNP during an episode (56.4±14.5) and those with CNP (56.1±19.5) was similar.

Descriptive statistics of self-reported questionnaire measured at baseline for the three groups are provided in Table 5.2. Quality of life by EQ-5D ($x^2(2) = 23.03$, $p<0.0001$) was significantly different across all three groups. Patients with CNP presented with the highest disability (17.5±7.6), followed by RNP (5.5±3.2), and healthy controls who had almost no disability as expected (0.7±1.1). The opposite was observed for quality of life where participants with RNP (0.92±0.09), and CNP (0.68±0.21) had significantly lower scores compared to healthy controls (0.98±0.04), indicating lower quality of life. The Tukey post-hoc comparison test revealed significant differences in TSK between those with RNP and healthy controls ($p<0.001$), and CNP and healthy controls ($p<0.0001$), but not between RNP and CNP (Table 5.2). Significant differences were observed for EQ-VAS between RNP and CNP ($p<0.05$), and between healthy controls and CNP ($p<0.001$).

Table 5.2: Baseline characteristics of all three groups

	Groups			p-value
	Healthy control (n=15)	RNP (n=22)	CNP (n=8)	
	Mean±SD	Mean±SD	Mean±SD	
Age (years)	31.1±5.7	31.0±11.8	33.6±8.7	0.24 [1]
Gender (male:female (%))	6:9 (60%)	8:14 (64%)	1:7 (88%)	0.38 [2]
Height (m)	1.7±0.1	1.7±0.1	1.6±0.1	0.02 [3]
Weight (kg)	69.1±14.8	74.7±18.0	59.5±9.8	0.07 [1]
NDI (0-50)	0.7±1.1	5.5±3.2	17.5±7.6	-
TSK (17-68)	29.1±4.3	35.2±5.5 *	40.5±7.5 *	<0.001 [3]
EQ-5D (0-1)	0.98±0.04	0.92±0.09 *	0.68±0.21 *†	<0.001 [1]
EQ VAS (0-100)	85.5±10.2	78.5±15.4	64.1±14.4 *†	0.005 [1]
Number of pain episodes, 12 m		5.9±4.4		
Average of pain episodes, VAS (0-100)		56.4±14.5		
Current neck pain, VAS (0-100)			56.1±19.5	
Neck pain duration, m			39.1±41.4	

SD: standard deviation; NDI: Neck Disability Index; TSK: Tampa Scale of Kinesiophobia; EQ-5D: European Quality of life – 5 Dimensions; EQ-VAS; self-rated health on a vertical visual analogue scale; VAS: Visual Analogue Scale.

1 Kruskal-Wallis Test
2 Chi-square Test
3 One-way ANOVA (Bonferroni post hoc shows significant group difference in height between healthy and CNP [p<0.02], and RNP and CNP [p<0.03])

* Post hoc significant difference from control group at p<0.05
† Post hoc significant difference from RNP group at p<0.05

5.4.2 Cervical kinematics and proprioception

The descriptive statistics and the results of the one-way ANOVA for cervical kinematics and proprioception are reported in Table 5.3. People with RNP showed no significant differences when compared to healthy or CNP groups in ROM, but significant differences were observed between CNP and controls in combined ROM in flexion and extension ($p<0.05$), and combined right and left rotation ($p<0.05$) (Appendix 36). JPE following right ($x^2(2) = 0.08$, $p=0.96$) and left ($x^2(2) = 0.58$, $p=0.75$) rotations were not significantly different among groups (Appendix 37).

Table 5.3: Summary statistics for the kinematic and proprioception features of all three groups with differences assessed using One-way ANOVA

	Groups			p-value
	Healthy control (n=15) Mean±SD	RNP (n=22) Mean±SD	CNP (n=8) Mean±SD	
Flexion				
Vmean (°/s)	72.8±12.3	55.0±18.5 *	42.9±14.3 *	0.002 [1]
Vpeak (°/s)	149.5±33.9	114.0±41.3 *	90.8±28.8 *	0.004
NVP (n)	9.4±4.0	17.1±9.4 *	17.5±8.2	0.005 [2]
Extension				
Vmean (°/s)	66.5±15.7	55.4±21.2	46.7±16.5	0.09 [1]
Vpeak (°/s)	133.8±31.5	111.0±45.1	97.2±34.4	0.12
NVP (n)	8.3±4.1	17.8±14.0	16.5±9.0	0.066 [1]
Right Rotation				
Vmean (°/s)	132.5±29.3	101.5±41.7 *	82.5±22.0 *	0.001 [2]
Vpeak (°/s)	244.7±52.5	190.5±76.7	157.1±37.9 *	0.001 [2]
NVP (n)	5.1±3.3	8.6±9.1	10.2±6.5 *	0.017 [1]
JPE	3.8±2.1	4.4±2.5	5.5±5.9	0.76 [1]
Left Rotation				
Vmean (°/s)	131.2±30.7	100.1±41.0 *	79.5±22.6 *	0.001 [2]
Vpeak (°/s)	244.5±57.2	188.8±71.7 *	148.7±34.7 *	<0.001 [2]
NVP (n)	3.7±2.8	9.0±8.8 *	11.6±10.5 *	0.014 [1]
JPE	4.2±2.8	4.7±2.8	5.2±5.2	0.711 [1]
Combined ROM				
Flexion/Extension	52.6±8.1	49.5±7.9	42.9±10.2 *	0.041
Right/Left Rotations	71.5±6.2	67.1±9.4	62.1±9.1 *	0.042

SD: standard deviation; ROM: Range of motion; Vmean: mean velocity; Vpeak: peak velocity; Vpeaks: mean of peaks velocity; NVP: number of velocity peaks; JPE: joint position error.

[1] Differences were assessed using Kruskal-Wallis ANOVA
[2] Differences were assessed using Welch's ANOVA
* Post hoc significant difference from control group at p<0.05

Mean velocity was significantly lower in those with RNP and CNP than healthy controls during neck flexion ($x^2(2) = 12.98$, p=0.0015) right rotation ($F(2,39) = 5.24$, p = 0.01), and left rotation ($F(2,39) = 5.53$, p = 0.008), but not during neck extension ($x^2(2) = 4.81$, p=0.09). Neither group with neck pain show significant differences in mean velocity during any movement direction (Figure 5.2).

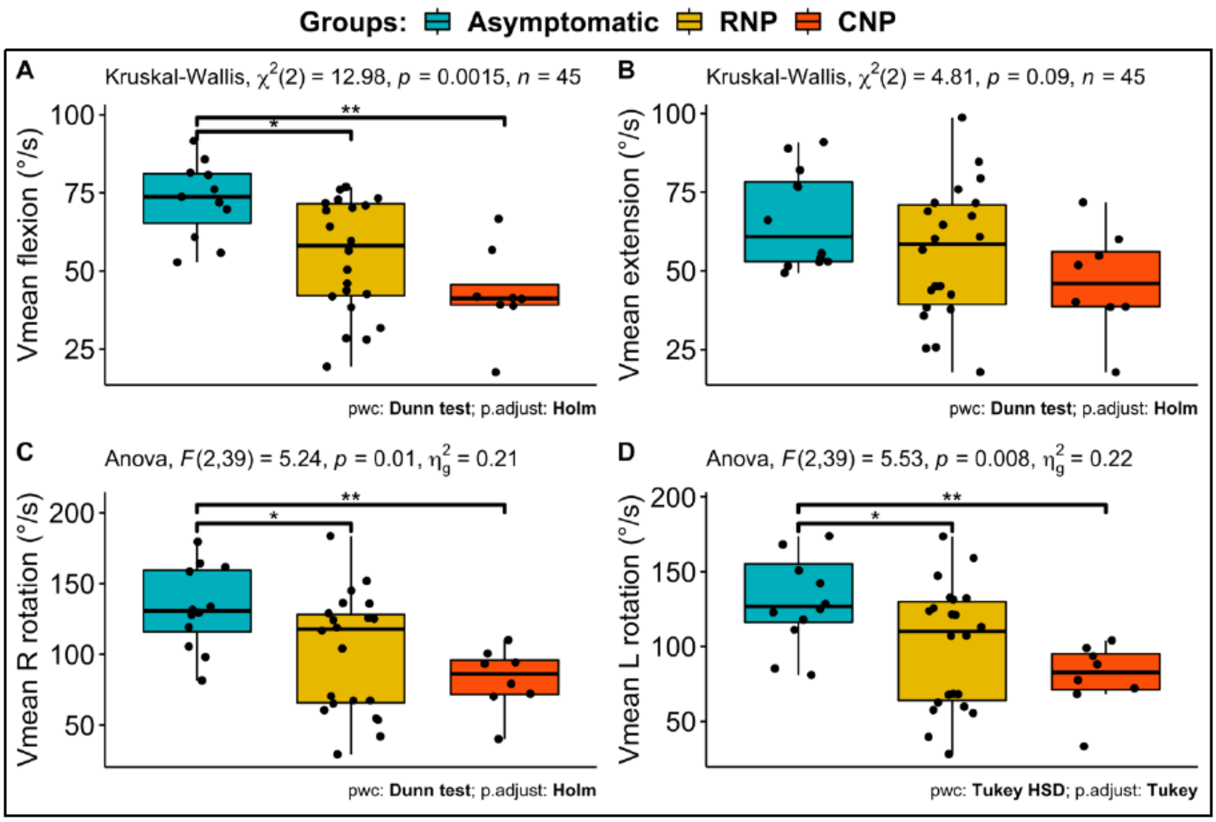

Figure 5.2: Box plots for mean velocity (Vmean) during neck movements in all directions

The NVP were higher (less smooth movement) in all directions in those with RNP and CNP compared to healthy controls (Figure 5.3). However, significant differences for the RNP group were only observed during flexion and left rotation ($p<0.05$), and during both rotations for those with CNP ($p<0.05$). Both groups with neck pain showed similar NVP with no significant difference between groups.

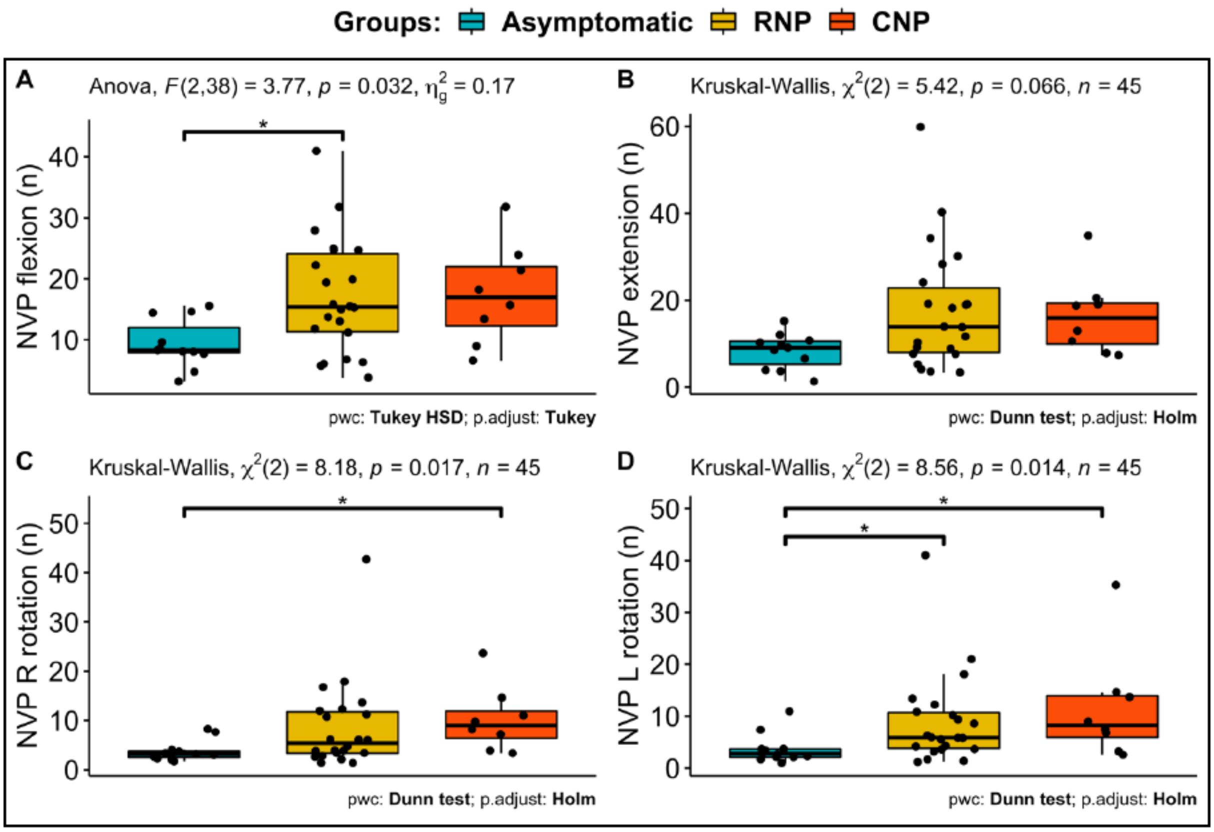

Figure 5.3: Box plots for number of velocity peaks (NVP) in all directions

5.4.3 EMG amplitude assessed during submaximal CCF contractions

A two-way ANOVA was performed to investigate the impact of group on the EMG amplitude of SCM at different force levels. The results showed a main effect of the group (F=8.34, p<0.001) on the EMG amplitude of the SCM muscle. The post-hoc analysis showed significant differences in EMG amplitude between the CNP group and the control group (p<0.001) and between the CNP group and the RNP group (p=0.02). However, no significant differences were found between the RNP group and healthy controls (p=0.10). The mean and standard deviations are summarised in Table 5.4.

Table 5.4: Mean and standard deviation of the normalized EMG amplitude (%) recorded from sternocleidomastoid muscles during each of the four submaximal cranio-cervical flexion contractions

	Groups		
	Healthy control (n=15) Mean±SD	RNP (n=22) Mean±SD	CNP (n=8) Mean±SD
Normalized EMG amplitude (%)			
20%	18.8±12.0	33.6±22.6	52.0±53.1
40%	35.2±23.9	64.3±88.5	70.8±36.5
60%	50.9±15.9	58.7±29.0	111.8±80.1
80%	66.9±21.7	79.0±33.6	108.6±88.4

SD: standard deviation; Numbers are presented as normalized EMG (%)

5.4.4 Maximal neck strength and perceived fatigue

A significant difference was observed between people with RNP and controls for neck extension strength (P<0.05), but with no significant difference between RNP and CNP groups. No difference in neck flexion strength was observed between groups. People with RNP and CNP displayed similar greater perceived exertion in flexion and extension. Perceived exertion assessed during the submaximal isometric neck flexion was significantly different between those with RNP and controls (p<0.01). Results are summarised in Table 5.5, and presented in Figure 5.4.

Table 5.5: Results of neck strength during the isometric contraction and perceived fatigue during submaximal contraction in MCU.

	Groups			
	Healthy control (n=15) Mean±SD	RNP (n=22) Mean±SD	CNP (n=8) Mean±SD	p-value
Maximal strength (MVC)				
Flexion MVC (kg)	20.2±9.7	14.6±6.4	15.3±3.1	0.17 [1]
Extension MVC (kg)	29.6±18.5	15.3±4.4 *	21.6±9.1	0.006 [1]
Rate of perceived exertion (BORG scale: 6 - 20)				
Flexion Borg (6-20)	12.0±3.1	15.0±3.0 *	14.7±1.7	0.01
Extension Borg (6-20)	8.9±2.5	9.9±2.5	10.4±2.6	0.38 [1]

SD: standard deviation; MVC: maximal voluntary contraction.
[1] Kruskal-Wallis ANOVA
* Post hoc significant difference from control group at *p*<0.05

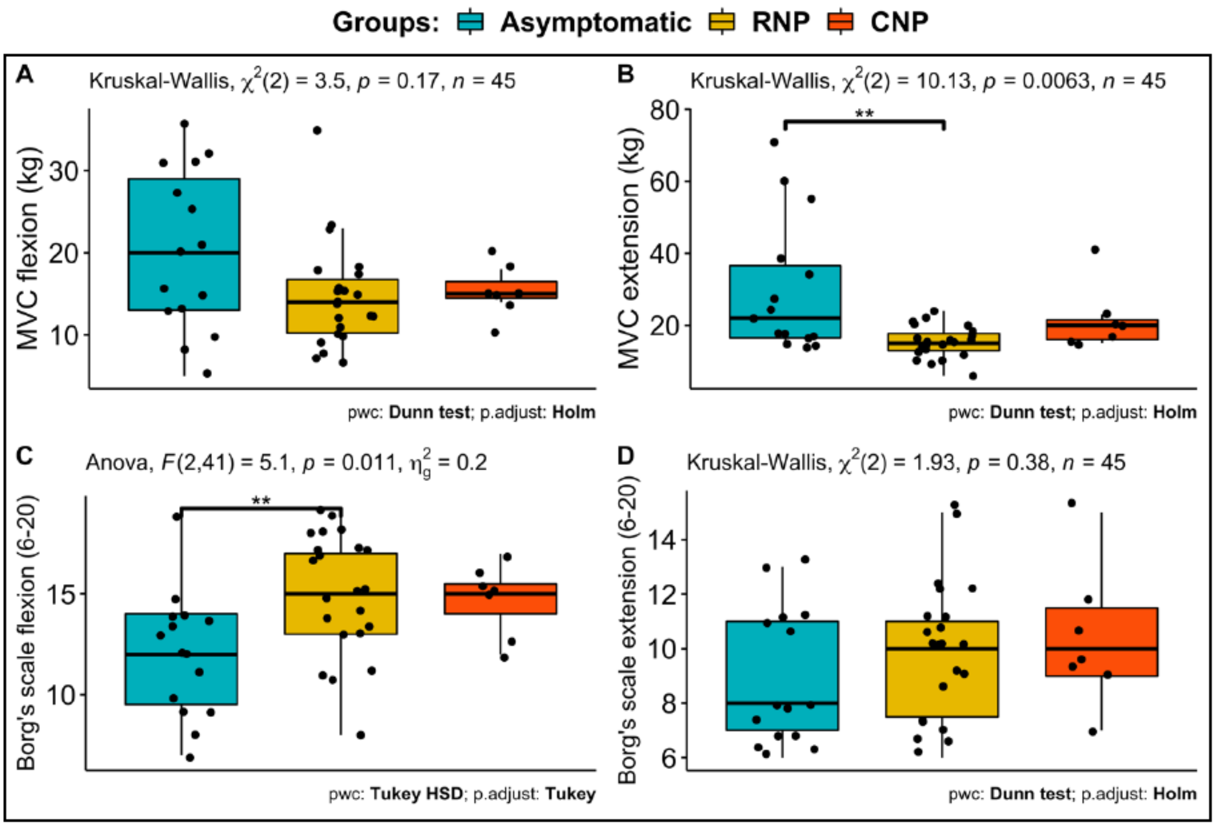

Figure 5.4: Box plots for maximal neck strength (MVC) and perceived fatigue

5.4.5 Participant follow-up through the longitudinal analysis

The total number of participants who completed the follow-up questionnaires at each month is reported in Figure 5.1. From 22 participants who participated at baseline, 17 (77%) participants completed the NDI at six months, whereas 19 (86%) completed the outcomes related to number days with pain.

Two participants did not complete any of the 12-month follow-up questionnaires despite the maximum of three reminders. The highest completion rate of follow-up was at the first month (n=20; 91%), whereas the lowest was at 12 months (n=16; 73%). One participant withdrew from the study at three months without providing any reason. No significant differences in baseline characteristics were present between the participants who dropped out and those included in the current study.

5.4.5.1 ***Characteristics of participants***

Self-reported outcomes indicated that, on average over the 12 months, people complained of neck pain for an average of five days per month. The mean of monthly number of days with pain for all participants is illustrated in Figure 5.5. Mean neck disability assessed by the NDI was (mean ± SD) of 8.6±5.0 at six months.

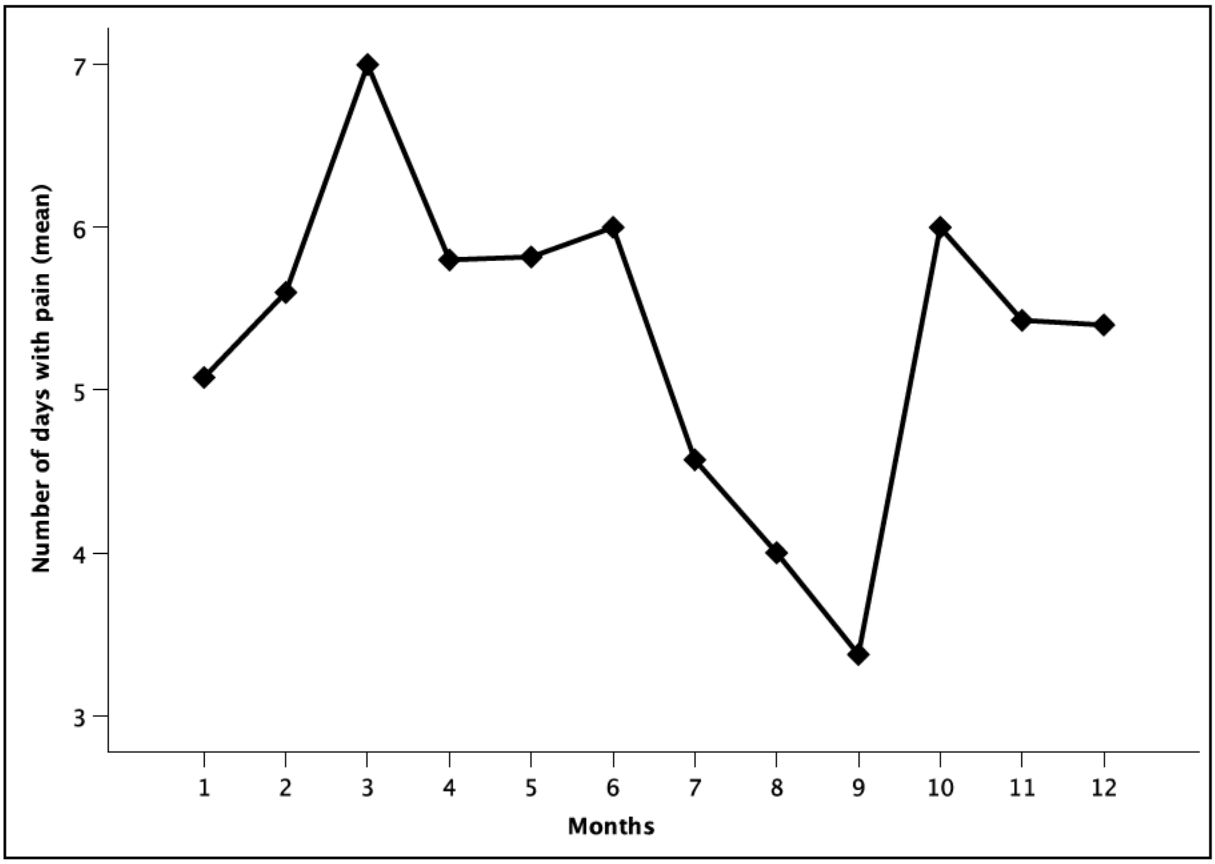

Figure 5.5: Mean values of number of days with pain over 12 months follow-up period

5.4.5.2 ***Step 1: Predictor Variable Selection (i.e., Shrinking the Number of Predictors)***

The baseline covariates for both outcomes (NDI and future episodes of neck pain) that had nonzero coefficients are reported in Table 5.6. Using LASSO, the number of predictors for the outcome NDI at six months was reduced from 15 to two predictors including MVC in flexion and previous number of days with pain. For predicting the outcome future episodes of neck pain at one year, the number of predictors was reduced from 15 to one which was previous number of pain episodes. These variables for the two outcomes were included in the multivariate regression analysis in the next step. A graph for the reduction in number of predictors achieved by applying LASSO are available in Appendix 38 and Appendix 39.

Table 5.6: Selected predictor variables for response variable of number of days with pain.

	NDI at six months	Number of days with pain
(Intercept)	8.65	4.68
NDI	0	0
TSK	0	0
EQ-VAS	0	0
EQ-5D	0	0
Previous number of pain episodes	0.68	0.57
Average of pain episodes	0	0
ROM in flexions and extension	0	0
ROM in rotations	0	0
NVP in flexions and extension	0	0
JPE	0	0
20% and 40 of CCF MVC force	0	0
60%, and 80% of CCF MVC force	0	0
CCF MVC	0	0
MVC during cervical flexion	-0.34	0
MVC during cervical extension	0	0

NDI: Neck Disability Index; TSK: Tampa Scale of Kinesiophobia; EQ-5D: European Quality of life – 5 Dimensions; EQ-VAS; self-rated health on a vertical visual analogue scale; ROM: Range of motion; NVP: number of velocity peaks; JPE: joint position error; CCF MVC: Maximum craniocervical flexion strength; MVC: maximal voluntary contraction.

5.4.5.3 ***Step 2: prediction models development***

5.4.5.3.1 Prediction of neck pain and disability at six months

A multiple regression was run to predict NDI at six months from MVC during flexion and previous number of neck pain episodes. These variables significantly predicted the NDI at six month, $F(2, 14) = 6.97$, p = 0.008, R^2=0.50. All two variables added significantly to the prediction model which are reported in Table 5.7. A one kg reduction in MVC in flexion significantly increased NDI by 0.32 units (t =-2.21, p=0.04, 95% CI: [-0.64]-[-0.01]). A single episode of neck pain within the last 12 months significantly predicted an increase in NDI by 0.54 unit (t =2.56, p=0.02, 95% CI: 0.09-0.99). This model explained 43% of the variability in NDI at six months. This model resulted in a RMSE of 3.47 meaning that the

NDI values that were predicted by this model differed from the observed values of NDI by 3.47 (Figure 5.6.A).

Table 5.7: results of multivariate regression analysis showing associations between baseline predictors and NDI at six months.

	β	SE	T Value	*p* Value	Low 95%CI	Upper 95% CI	Adjusted R2
(Intercept)	10.23	2.99	3.42	0.004	3.82	16.63	0.43
MVC flexion	-0.32	0.15	-2.21	0.04	-0.64	-0.01	
Previous number of pain episodes	0.54	0.21	2.56	0.02	0.09	0.99	

β: Unstandardized Coefficient; SE: Standard Error; CI: Confidence Intervals; Adjusted R2: represents the variance in NDI (the outcome) as explained by the variables; MVC: Maximum Voluntary Contraction.
n=19; 86%; with complete cases

5.4.5.3.2 Prediction of future episodes of neck pain over the 12-month follow-up period

A multiple regression was run to predict future episodes of neck pain within the next year, from previous number of pain episodes. This variable resulted in a statistically significant model predicting future episodes of neck pain, $F(1, 17) = 6.93$, $p = 0.017$, R^2=0.29. A single episode of neck pain within the last 12 months significantly predicted a future episode by 0.40 unit (t =2.63, p=0.02, 95% CI: 0.08-0.71) (Table 5.8). This model explained 25% of the variance in future episodes of neck pain. The RMSE for this model was 2.72, representing the differences in number of days between the predicted and observed values (Figure 5.6.B).

Table 5.8: results of multivariate regression analysis showing associations between baseline predictors and number of days with pain (average of 12 months)

	β	SE	T Value	*p* Value	Low 95%CI	Upper 95% CI	Adjusted R2
(Intercept)	2.14	1.17	1.83	0.08	-0.33	4.61	0.25
Previous number of pain episodes	0.40	0.15	2.63	0.02	0.08	0.71	

β: Unstandardized Coefficient; SE: Standard Error; CI: Confidence Intervals; Adjusted R2: represents the variance in number of days with pain (the outcome) as explained by the variable.
n=17, 77%, with complete cases

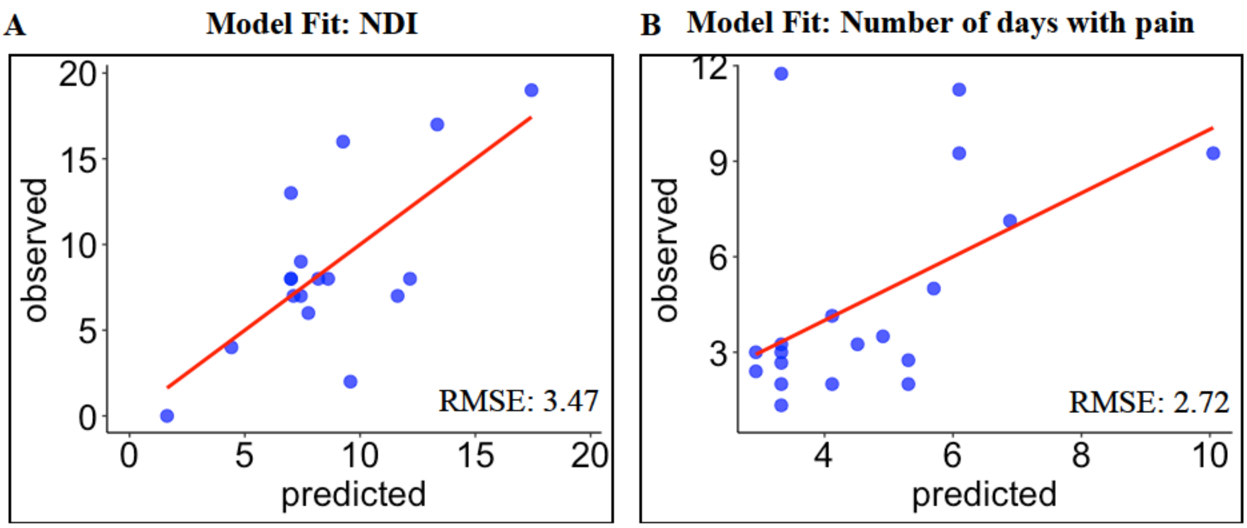

Figure 5.6: Scatterplots of two models fit comparing the predicted and observed values for each outcome: NDI: Neck disability index at six months (A) and number of days with pain over the 12-month follow-up period (B).

5.5 DISCUSSION

This is the first study to conduct a comprehensive investigation of neuromuscular features including cervical kinematics, sensorimotor performance (proprioception), superficial neck muscle activity, neck strength, and subjective fatigue among individuals with CNP, RNP (following a whiplash injury), and healthy controls. The findings provide evidence that people with a history of neck pain, even when in remission from pain, present with similar psychological and neuromuscular function consisting of altered neck movement, increased activity of superficial neck muscles, lower neck muscle strength, and greater perceived fatigue during sustained contractions. Importantly, when examining the predictive capacity of these features, lower neck flexion strength together with a higher number of previous pain episodes within the last 12 months were predictors of higher neck disability at six months. This provides preliminary evidence that some aspects of neuromuscular function (namely lower neck strength) are relevant for predicting future neck pain and disability.

The current study showed that people with either CNP or RNP following a whiplash injury, presented with higher kinesiophobia, and lower quality of life compared to healthy controls. The presence of psychological features and poorer quality of life have been commonly reported previously for patients with chronic WAD (Sterling and Chadwick, 2010) although, this is the first study to demonstrate that people with frequent episodes of neck pain could present with poorer quality of life and some degree of kinesiophobia despite being pain free.

5.5.1 Cervical ROM

In comparison to healthy controls, individuals with CNP showed a reduction in ROM in all directions. Reduced ROM either in all or some directions has been reported previously in patients with CNP (Baydal-Bertomeu et al., 2011), despite methodological differences between studies. Whilst not significant, the average cervical ROM was lower in people with RNP compared to the controls. The extent of restricted cervical ROM in people with RNP has not been studied before (Devecchi et al., 2021), but restricted ROM in the thoracic and lumbar spine was reported in people with recurrent LBP (Crosbie et al., 2013, Fenety and Kumar, 1992, Phillips, 2013). However, unlike the current study, the studies on recurrent LBP included participants that reported some degree of pain during the assessment (Crosbie et al., 2013, Phillips, 2013). Future research should further investigate the presence of changes in spine kinematics in people with RNP (Devecchi et al., 2021) in a larger sample size.

5.5.2 Velocity and smoothness of neck movement

Individuals with CNP in the current study moved their neck slowly and with irregular movements when performing cervical rotations. These findings are similar to previous work showing that people with CNP either from traumatic or non-traumatic causes, display more irregular and slower neck movement (Moghaddas et al., 2019, Salehi et al., 2021, Baydal-Bertomeu et al., 2011, Sjölander et al., 2008). Such a pattern of movement could be interpreted as cautious movements to avoid neck pain (Hodges and Tucker, 2011). These changes in how neck movements are performed are in line with current theories regarding how pain affects movement and motor control (Hodges and Tucker, 2011). However, the current study uniquely showed that slower neck movement in flexion and rotation with irregular neck movements in flexion and left rotation can also be present even when pain is not present, i.e., during a period of remission in people with RNP. The driving mechanism for the altered movement performance (slow and irregular movement) during pain remission is not fully understood and further studies exploring these neuromuscular adaptations and their association to clinical features should be investigated.

5.5.3 Cervical proprioception

The observed alteration in the smoothness of movement in individuals with CNP and RNP suggests that JPE may be disturbed in those groups. This is because cervical proprioceptive information plays a vital role in enabling precise head movements (Röijezon et al., 2015). Moreover, individuals with neck pain tend to experience diminished proprioceptive input acuity, affecting the accuracy and fluidity of their movements (de Vries et al., 2015, Revel et al., 1991). However, even though significant differences in smoothness of neck movement were observed, JPE during cervical rotation did not show significant differences among the groups in this study. This finding was also observed in previous studies of patients with persistent WAD, who have similar pain intensity to the cohort tested in the current study (De Pauw et al., 2018, Treleaven et al., 2008, Woodhouse and Vasseljen, 2008b).

A recent meta-analysis, found that patients with chronic WAD have significant larger JPE following cervical rotation when compared to healthy controls, but there is discrepancy between studies (Mazaheri et al., 2021). Such discrepancies could be attributed to various factors. For example, several studies have used different methods to assess JPE including a variety of measurement devices and sensor placements (de Vries et al., 2015) that potentially influenced the findings. Moreover, people with chronic WAD presenting with dizziness or greater pain intensity tend to show greater deficits in sensorimotor control (Treleaven, 2011), and this was not accounted for in current study. Finally, sensorimotor disturbances are highly variable between people with WAD in both the nature of impairments and their frequency of presentation (Treleaven, 2011) and thus our sample size may have not been sufficient to capture a difference.

5.5.4 EMG amplitude assessed during CCF submaximal contractions

The findings of this study showed that individuals with CNP exhibited altered muscle activation patterns compared to healthy controls during the performance of CCF. Specifically, a higher activity of the SCM in people with CNP compared to healthy controls was observed which may be indicative of compensatory strategies or changes in motor control strategies due to the presence of pain. Previous studies showed that people with CNP often display higher activation of the superficial neck flexors (Falla et al., 2004a, Falla et al., 2004b, Falla et al., 2004d, Jull et al., 2004), which is negatively associated with the extent of activation of the deep neck flexors (Jull and Falla, 2016). The effect of pain on coordination between the deep and superficial neck flexors is well documented (Falla et al., 2007b, Falla and Farina, 2008, Falla et al., 2007a), and such a phenomenon was also seen early in patients with acute neck pain following a whiplash trauma (Sterling et al., 2003b).

5.5.5 Maximal neck strength and perceived fatigue

Both groups with a history of neck pain displayed lower isometric neck flexion and extension strength, although significant differences were only observed in extension between people with RNP and controls. People with neck pain frequently present with lower neck strength (Cagnie et al., 2007, Pearson et al., 2009, Scheuer and Friedrich, 2010, Ylinen et al., 2004), though the degree of impairment varies greatly between patients (Ylinen and Ruuska, 1994) and can be associated with features such as the degree of kinesiophobia (Lindstroem et al., 2012) and current pain intensity (Jull et al., 2018). Previous work has shown that, compared to healthy controls, individuals with persistent WAD have significantly lower isometric MVC force in extension, retraction, and lateral flexion (Pearson et al., 2009). However, the current study was not able to confirm these findings. These differences could be explained due to the natural variability of neck strength among participants (Hodges and Tucker, 2011), with a large range of neck strength values shown in people with CNP previously, most likely reflecting the large heterogeneity observed between people with neck pain (Kumbhare et al., 2005, Prushansky et al., 2005, Descarreaux et al., 2007, Pearson et al., 2009). Another reason could relate to the level of disability since strength deficits are typically larger in those with higher disability (Pearson et al., 2009).

The study found that individuals with RNP and CNP had weaker neck flexor strength by about 5 kg and weaker neck extensor strength by about 10-15 kg compared to healthy controls. As discussed in section 1.2.2, page 6, the sudden stretching of the neck muscles during the whiplash motion can cause larger strains in the superficial posterior neck muscles, such as the semispinalis, splenius capitis, and upper trapezius (Vasavada et al., 2007). In addition, other soft tissue injuries in the back of the neck, such as injuries to the ligaments, discs, and facet joints, may contribute to weakness of the neck extensors (Elliott et al., 2009). Overall, these findings highlight the importance of targeted rehabilitation programs that focus on strengthening the neck muscles to improve functional outcomes and reduce symptoms in individuals with WAD.

The findings from this study indicate that individuals with RNP experienced significantly higher perceived fatigue during neck flexion at 25% of MVC compared to healthy controls. Although fatigue was measured subjectively in this study using Borg's scale, findings from studies using myoelectric manifestations of fatigue may provide an explanation for this observation. Despite being pain-free during assessment, the presence of fatigue in people with RNP could be linked to long-lasting adaptations affecting muscle properties, as noted by Falla et al. (2008). The authors indicated that increased muscle fatigue during sustained isometric contractions may be due to histological and morphological changes in the cervical muscles, likely resulting from long-term adaptations to the modified motor control strategies.

5.5.6 Predicting neck disability and number of days with pain

In our sample, higher number of pain episodes within the last 12 months was a common predictor of higher neck disability and a higher number of days with pain. This finding is consistent with a previous prognostic study of people with RNP who were followed for one year (Langenfeld et al., 2015). The study found that a previous episode of neck pain predicted future recurrence of pain, which was defined as a new episode of neck pain (Stanton et al., 2011). Another study in people with LBP confirmed the negative effect of a longer duration of a current episode on disability up to five years (Enthoven et al., 2006). Nonetheless, no study has investigated this in people with RNP following a whiplash trauma, which warrants further investigation.

Lower isometric neck strength in flexion was identified as a predictive factor of higher disability at six months, even though there were no significant differences in neck flexion strength between the groups at baseline. While not directly comparable to the current study, previous studies found similar findings in that muscle strength was a significant factor predicting future injury in the lower limb (Croisier et al., 2008, Cronström et al., 2016, Fousekis et al., 2011, Ryan et al., 2014). These findings could emphasize the potential long-term effect of impaired neck strength and frequent episodes of neck pain on the development of neck disability. Further studies need to confirm this finding and investigate the interaction between neck muscle strength and future episodes of neck pain.

5.5.6.1 ***The performance of our models***

In this study, our models performed similarly to earlier machine learning prediction models. The first model in this study provided an estimate of the expected NDI values at six months with an average RMSE of 3.47 points, on a 0-50 scale. This score represents the average magnitude (error) of the difference between the observed NDI at six months and scores predicted by the model. In another words, it measures how close the observed data points are to the predicted model values where lower RMSE values reflect a better fit.
The RMSE score to predict NDI is similar to a model generated in people with cervical radiculopathy (Liew et al., 2020a), with RMSE of about 8.2% (NDI 0-100% scale). However, this comparison should be interpreted with caution due to different population. The other developed model in the current study showed that average differences between predicted and observed values, indicated by RMSE, was 2.72 days with pain.

5.5.7 **Clinical implications**

The current study provided evidence that people with RNP presented with changes in some neuromuscular and psychological features even during complete remission of pain. Furthermore, some of these changes were comparable to people with CNP. These findings could have significant implications for rehabilitation and prevention. For example, some of the features could be targeted in a rehabilitation program with the aim to promote restoration of altered function identified in this study and preventing recurrent episodes of neck pain. Commonly treatment is aimed at reducing pain, yet this work emphasises that restoration of neuromuscular function is equally relevant.

The longitudinal investigation in the current study showed that a higher number of previous pain episodes together with lower neck flexion strength predicted higher neck disability six months later. Neck strength is a modifiable feature. Thus, strengthening of the neck flexors in people with RNP may lower future neck disability although this needs to be tested in a longitudinal study. On the other hand, although the number of previous pain episodes is not a modifiable variable, this should be considered.

5.5.8 Strength and limitations

This study has several strengths. This is the first study to examine physical features in a group of participants with RNP following a whiplash injury who were asymptomatic at inception. Moreover, a comprehensive battery of measures including demographic, psychological, and physical features were assessed at baseline. All these baseline features were then included as predictors of outcomes in people with RNP who were followed up over 12 months. A follow-up rate of more than 80% is desired in prognostic research (Linton et al., 2005). This cut-off was fulfilled in one of the developing models including 86% follow-up rate across 12 months study period. For prognostic analysis, best practice recommendations were followed for the development and validation of the models (Moons et al., 2015, Steyerberg et al., 2013).

There are some limitations to consider. One of the main limitations of this study is the small sample size which might bias the results of this study. A sample size of 50 participants for RNP, 15 for CNP, and 15 for controls was planned in advance, but this was fulfilled only in the latter group. This was because of the COVID-19 pandemic which interrupted data collection. However, the current study was able to find some significant differences across groups and/or show a trend at baseline. Another potential limitation is that the number of female participants was higher than the male in the group with CNP. However, no significant differences were observed in gender across groups as reported in Table 5.2, page 138. For prognostic analysis, a low sample size in the RNP group prevents us from separating the data into training and validation sets, the latter could be used in independent validation (Steyerberg et al., 2013). Furthermore, this smaller sample size compared to the high number of predictors could lead to overfitting of the developed models. However, this study incorporated LASSO, a powerful method that performs regularization and feature selection and can deal with a high number of predictors (Fonti and Belitser, 2017). This is a unique study, but it is difficult to determine the extent to which the results are generalizable, especially given that a convenience sample was adopted. Additionally, this study may not be generalizable to people with greater neck pain and disability as this was associated with general variability of neuromuscular adaptations (Falla et al., 2004a, Falla et al., 2011, Lindstrøm et al., 2011). This study included people with RNP and CNP who experienced minimal and mild to moderate pain and disability (Sterling et al., 2005), respectively. Similarly, the higher level of kinesiophobia in people with CNP in the current study may not be generalizable to other cohorts with CNP who present lower levels of kinesiophobia. Restriction in the range and performance of neck movements could be influenced by kinesiophobia (Bahat et al., 2014a, Pool et al., 2010), which is the only measure of psychological function that was assessed in the current study.

5.6 CONCLUSIONS

Participants with RNP during a period of remission presented with altered neuromuscular function and poorer psychological function, and several of these features were comparable to the presentation of people with CNP. These features included higher disability, higher kinesiophobia, and lower quality of life. People with RNP also performed slower and more irregular neck movements in most directions and displayed lower neck strength in extension and higher perceived fatigue in flexion. Some of these baseline variables were able to predict ongoing neck disability and days with pain in those with RNP when followed over 12 months. These included a higher number of previous pain episodes and lower neck flexion strength. This work emphasises that neuromuscular function restoration is as important as pain relief when managing people with neck pain.

CHAPTER 6

GENERAL DISCUSSION

6.1 Summary of findings

In this thesis, the primary aim was to determine whether people with acute, recurrent and CNP after a whiplash trauma present with altered cervical kinematics, neuromuscular function or psychological function and to explore their relevance to ongoing pain and disability for people with acute WAD and RNP. A cross-sectional analysis and a longitudinal analysis were adopted to investigate this aim.

Chapter One provided a general overview of the prevalence, significance and classification of neck pain disorders. Further background details specific to WAD were then introduced, including WAD's clinical manifestation throughout the acute, recurring and chronic stages. For example, self-reported symptoms related to pain and psychological distress were highlighted, along with information about physical signs following a whiplash injury, such as movement dysfunctions, sensorimotor disturbances and neuromuscular adaptations. The chapter then continued to document the current evidence on the predictive factors for the chronicity and recurrence of pain, as well as the current challenges in the field of WAD. Areas of the body of research that have not been fully examined were identified and determined as the objectives of this thesis.

An observational case-control study was presented in Chapter Two, aiming to investigate whether measurements of cervical kinematics are modified in individuals with acute WAD and whether these changes are related to self-reported outcomes (Alalawi et al., 2022c). Evaluations of cervical kinematic features have clinical value, since they may be used as targets for rehabilitation programmes. Individuals with acute WAD were recruited for this study within 15 days of a car crash, along with healthy controls. During the performance of active neck movement, kinematic measures were collected, including ROM, velocity and smoothness of movement and JPE. In comparison to healthy controls, all features of cervical kinematics (such as ROM, mean and peak velocity and smoothness of movement) were altered. Twelve of the 18 kinematic measures had significant associations with the self-reported measure NDI, but none of those characteristics were linked to kinesiophobia. Since most of the altered cervical kinematics features were associated with disability soon after the injury, the next chapter evaluates whether the predictive ability of these features in people with WAD has been previously explored.

Chapter Three provided a systematic review to summarise the existing evidence on cervical kinematic parameters' capacity to predict the persistence of pain and disability following a whiplash injury (Alalawi et al., 2022d). A high WAD grade and greater pain-related impairment were predictors of poor outcomes. Neck ROM, JPE, superficial neck muscular activity, neck muscle strength/endurance and perceived functional ability may not be predictive of outcomes, according to inconclusive evidence. The ability of cervical kinematics parameters such as the velocity of neck movement, smoothness of motion and coactivation of neck muscles to predict outcomes following a whiplash injury has not been evaluated before, warranting further research in this area. Thus, the next chapter examined whether physical features related to neck movement can predict ongoing pain and disability for individuals with WAD six months post injury.

Chapter Four presented a preliminary longitudinal study to investigate the association between cervical kinematic features collected at baseline (i.e., reported in Chapter Two) (Alalawi et al., 2022c) and the presence of persistent pain and disability six months post injury in individuals with WAD. All baseline features of cervical kinematics during neck extension were significantly associated with the level of perceived disability (using the NDI) at six months post injury. Additionally, pain catastrophising showed a significant correlation with the NDI six months after injury. This is the first study to provide preliminary evidence about the association between movement characteristics in extension and pain catastrophising with ongoing pain and disability six months following a whiplash injury. This may indicate that rehabilitation programmes aimed at their alteration may aid in the prevention of chronicity in such populations.

Neck pain is characterised by a high recurrence rate, as indicated in Chapter One, section 1.3.7.1, page 28. Even when pain is resolved, some measurements of neuromuscular function might not return to the levels seen in healthy individuals (Jull et al., 2002, Sterling et al., 2001). A comprehensive assessment of physical and psychological features, involving the examination of neck movements, proprioception, the activity of superficial neck muscles, neck strength and fatigue, is needed. Knowledge of these features could improve our understanding of the ongoing features present during remission and could have significant implications for the prevention and rehabilitation of RNP.

Chapter Five was a cross-sectional and longitudinal analysis aiming to determine if there are any differences between healthy controls and those with RNP or CNP in cervical kinematics, neuromuscular function and psychological function (Alalawi et al., 2022a). A secondary goal was to explore whether these features could predict future pain recurrence in individuals with RNP. Similar characteristics, such as greater neck disability, increased kinesiophobia, reduced quality of life, slower and more irregular neck motions and less neck strength, were evident in both the RNP and CNP groups. In individuals with RNP, greater neck disability at a six-month follow-up was predicted by a greater number of prior pain episodes over the previous 12 months and lower neck flexion strength (Alalawi et al., 2022a). Chapter Five provides evidence that people with RNP, even when in remission from pain, present with ongoing impartments in psychological and neuromuscular function similar to those found in people with CNP. Of these ongoing features, low neck strength predicted the future recurrence of neck pain.

6.2 Physical features in the presence and absence of pain

As previously indicated in the introduction of this thesis, the presence of movement dysfunctions, such as restricted neck movement and cervical proprioception in people with RNP, together with velocity and smoothness of movement in people with acute WAD and RNP, has not been studied before. In addition, several neuromuscular adaptations have not been considered in people with RNP, and they deserve further investigation in people with acute WAD and CNP. These include features related to muscle strength, endurance, fatigue and the activity of superficial neck flexors. Three empirical studies were carried out to bridge the gap in the current knowledge regarding whether disturbed physical features exist in people with traumatic neck pain at different pain stages.

6.2.1 Physical features of people with acute or CNP

In this thesis, a consistent pattern of altered cervical movements was identified in people experiencing neck pain following a whiplash injury (Alalawi et al., 2022a, Alalawi et al., 2022c). This was characterised by a reduced range of cervical movements in people with acute (Alalawi et al., 2022c) and chronic WAD (Alalawi et al., 2022a) when they performed continuous neck movement during flexion and extension. In addition to the reduced movement, the findings reflected in Chapter Two showed that people with acute WAD moved their necks slowly and with irregular movement in all directions compared to healthy controls (Alalawi et al., 2022c). In Chapter Five, similar observations of slower (all directions except in extension) and irregular neck movement (during neck rotations) were also seen in people with CNP compared to healthy controls (Alalawi et al., 2022a). Considering all the evidence gathered from Chapters Two and Five, the data suggest significant changes in features of physical function when performing active neck movements, which exist soon after a whiplash injury. In addition, disturbances in the physical function of movement remain disturbed in people with CNP (Alalawi et al., 2022a), as seen in Chapter Five.

Similar patterns of musculoskeletal impairments have been observed in other populations, such as people with idiopathic neck pain, headaches and mild concussions. For example, the characteristics of cervical kinematics (e.g. range and smoothness of movement) were evaluated in patients with idiopathic CNP and compared to matched healthy controls when performing functional tasks (Moghaddas et al., 2022). Four functional tasks, including fastening a seatbelt and reaching tasks involving forward, right or left movement while standing, were carried out. These movements are typically painful for patients with neck pain. Participants with CNP had lower total 'head + neck upper trunk' movement in all tasks and higher NVP in flexion compared to controls. This is in line with the findings of this thesis, since it showed that patients with CNP performed their neck movements with less ROM and less smoothness.

Cervical impartments, such as ROM, the activity of superficial neck flexors and neck flexor and extensor strength, have been assessed in people with different types of headaches (Liang et al., 2019). Pooled data showed that ROM was significantly reduced in people with migraine and tension-type headaches compared to healthy controls (Liang et al., 2019). The activity of superficial neck flexors was assessed when performing the CCF test in people with headaches, with no significant differences seen in the migraine group compared to the healthy control group. Finally, neck strength in flexion and extension was not significantly different between people with headaches and controls, although heterogeneity among studies is high (Liang et al., 2019).

In addition, cervical kinematics, proprioception and endurance were assessed in people with mild traumatic brain injury (Galea et al., 2022). Recent evidence has shown that individuals with neck pain following a whiplash injury and mild traumatic brain injury have similar symptoms, biomechanics, cognitive disorders (Gil and Decq, 2021) and neck disability (Galea et al., 2019). In this study, patients who experienced neck pain as a result of trauma (mild concussion) were subgrouped into symptomatic and asymptomatic groups based on whether they experienced symptoms and their pain intensity at assessment (Galea et al., 2022). Individuals who reported ongoing symptoms with 1/10 (or more) on the VAS were categorised into the symptomatic group (Galea et al., 2022). Compared to healthy controls, individuals who had symptoms from one to six months after a mild concussion had deficits in cervical spine movement and sensorimotor features. This included reduced ROM in flexion and total rotations, as well as a reduced velocity of movement during rotation and lower cervical flexor endurance (Galea et al., 2022). The disturbances seen in people with head trauma were also seen in people in the acute and chronic stages following a whiplash injury in this thesis. Interesting findings from this population with mild concussions are that asymptomatic individuals, even if they are pain free, have some of the deficits seen in healthy controls, an observation that was seen in people with WAD (Alalawi et al., 2022a).

6.2.2 Physical features in people with previous neck pain episodes, but examined during a period of remission

Interestingly, in Chapter Five, similar ongoing movement dysfunctions, as well as neuromuscular adaptations in people with RNP, were also observed, even when they were pain free at inception (Alalawi et al., 2022a). For example, reduced motion, although not significant, slower velocity and irregular neck movement were all altered in people with RNP in almost all directions (Alalawi et al., 2022a). Additional features were assessed in this study, including the activity of superficial neck flexors and the strength and endurance of neck flexors and extensors (Alalawi et al., 2022a). Even though they were pain free, people with RNP showed similar disturbances to people with ongoing CNP in terms of physical and psychological function (Alalawi et al., 2022a). Thus, this could indicate that factors other than pain may contribute to the presence of ongoing neuromuscular disturbances in people with RNP.

6.2.2.1 ***Movement dysfunction***

Several movement kinematics were also seen in individuals with recurrent pain due to other musculoskeletal disorders. While the reduction in ROM was not statistically significant in people with RNP (Alalawi et al., 2022a), other studies of RNP and other musculoskeletal disorders have shown the opposite. For example, the cervical ROM of the thoracic and lumbar spine, which was assessed extensively, was found to be reduced during spinal movement in people with recurrent LBP (Devecchi et al., 2021). Similarly, when assessed during remission, people with RNP originating from a mild concussion demonstrated a significant reduction in cervical ROM during rotation (Galea et al., 2022). Adaptations in movement behaviour tend to be less severe during the remission period compared to individuals with ongoing symptoms, suggesting that they may be clinically relevant in some individuals but not in others (Galea et al., 2022).

Other movement dysfunctions related to the velocity and smoothness of movement were not previously assessed in patients with RNP (Devecchi et al., 2021), and this thesis was the first to assess these dysfunctions in people with a previous whiplash injury but tested during a period of remission. Very few studies have assessed movement velocity and smoothness in other musculoskeletal disorders. Slower trunk movement was observed in individuals with recurrent LBP when performing functional activities (reaching) (Crosbie et al., 2013) and when performing short-term movement choreography (Vaisy et al., 2015).

Viggiani et al. (2020) explored smoothness of movement (assessed by the root-mean-square of the angular jerk) in people with recurrent LBP. The study found greater irregular movement of the trunk when returning to a neutral standing position from full extension in recurrent LBP patients compared to healthy controls (Viggiani et al., 2020).

6.2.2.2 ***Neuromuscular performance***

The neuromuscular performance of individuals with idiopathic recurring LBP was previously evaluated in terms of muscle strength and endurance. The findings in Chapter Five indicate that people with RNP exhibited lower strength of their neck extensors compared to healthy controls (Alalawi et al., 2022a). Contrary to this finding, the strength of trunk extensors was not significantly different in another population of people with recurrent LBP when compared to healthy controls (Applegate et al., 2019). The inconsistent results may be explained by the differences between the two populations and the methods used to measure strength.

Another finding in Chapter Five is that people with RNP perceived significantly greater effort when performing isometric neck flexion compared to health controls (Alalawi et al., 2022a). This is in line with results from a group of people with recurrent LBP who reported greater perceived exertion than healthy controls, assessed by the Borg scale, when performing a low-load trunk extension exercise (D'hooge et al., 2013).

6.3 Predictive ability of physical factors in the transition to chronicity and pain recurrence

Chapter One of this thesis identified two challenges in the current literature around the predictive factors of ongoing and recurrent pain. The first challenge is that, while several disturbances in the features of physical function have been documented in people with WAD, there is very limited evidence about their predictive ability. Of the assessed features, only the

ROM's capacity for prediction and the activity of the superficial neck flexors were evaluated. Thus, the capacity of other physical characteristics to predict ongoing pain and disability in acute WAD is required.

The second challenge is that the recurrence of pain, in general, is common in individuals with neck pain (Shih et al., 2021). To reduce the recurrence rates of neck pain, it is argued that it is necessary to shift the current focus of the model of care to physical rehabilitation instead of focusing only on pain relief (Jull et al., 2018). The development of effective physical rehabilitation is hampered by a lack of established predictive factors for future pain recurrence (Da Silva et al., 2017). Thus, the investigation of the predictive capacity of a variety of measures in people with RNP during their remission periods is important and was therefore explored in this thesis.

6.3.1 Predictive ability of physical factors in the transition to chronicity

In Chapter Four, preliminary findings show that individuals with greater levels of pain and disability, as determined by the NDI after six months, have restricted neck movement, slower rates of movement, jerkier movements and greater levels of pain catastrophising when tested during the acute phase following recent whiplash injuries. This suggests that ongoing poor outcomes in people with WAD may be associated with early clinical features of disturbed physical and psychological functions. However, these are merely early findings from a correlation analysis; therefore, further research is needed to explore and determine their predictive abilities. This is the first study to assess the relevance of contemporary physical factors to ongoing poor outcomes in people with WAD. Thus, a comparison with similar literature is not possible.

The findings from Chapter Four provide preliminary indications about the association between catastrophising and poor outcomes following a whiplash injury. There is inconsistent evidence about the association between pain catastrophising and poor outcomes in people with WAD. This has been highlighted in a systematic review in which three studies found such an association, while the other two studies did not (Luque-Suarez et al., 2020). However, a meta-analysis revealed that greater levels of pain-related fear, catastrophising and depression were substantially linked to lower spinal movement amplitudes and increased muscular activity, even when controlled for pain intensity (Christe et al., 2021). Moreover, people with chronic WAD who had dizziness at 12 months were found to have greater levels of pain catastrophising compared to individuals with no dizziness (Treleaven et al., 2022).

6.3.2 **The predictive ability of physical factors for neck pain recurrence**

In Chapter Five, the regression analysis shows that when testing individuals with RNP during their remission period, the presence of lower neck flexion and a greater prior number of neck pain episodes can predict the recurrence rate of neck pain during the next 12 months (Alalawi et al., 2022a). This is the first study to show the predictive capacity of these features. This suggests that ongoing reduced muscle strength in neck flexion exists in people with RNP and has the potential to predict future recurrences and ongoing neck pain, even when individuals have no pain at inception.

Consistent with the evidence from this thesis, studies of patients with LBP showed that previous frequent episodes of pain were a consistent predictor of future recurrent episodes of LBP (Machado et al., 2017, Da Silva et al., 2017). Novel findings from this thesis determined the predictive ability of neck flexor strength on pain recurrence (Alalawi et al., 2022a), which is a modifiable factor. Another important aspect of this thesis is that individuals with RNP exhibit disturbed psychological function in addition to physical function, as previously reported (Alalawi et al., 2022a). Collectively, the findings from this thesis improve our understanding of the presence of physical and psychological disturbances in people with RNP and their relevance to recurrent episodes of neck pain.

Although not directly comparable to a population with RNP, a previous study of people with chronic WAD explored the predictive ability of muscle function on dizziness at a 12-month follow-up (Treleaven et al., 2022). The logistic regression analysis revealed that the endurance of neck muscle flexors and NDI were significantly associated with the presence of dizziness at 12 months following a general exercise intervention. This model accounts for 50% of the variations in dizziness.

Similar to our study, regarding people with idiopathic neck pain, Shahidi et al. (2015) assessed the predictive ability of psychological and physical features on the development of the first episode of neck pain in healthy individuals working in high-risk occupations. The outcome of interest was defined as neck pain greater than or equal to five on the NDI that had been maintained for at least three months. Some of the assessed psychological measures were depression, anxiety and catastrophising. In addition, physical measures included head posture, ROM in all directions, endurance (time to task failure) and strength (by a handheld dynamometer) of the neck flexors and extensors. The study found that 20% of the participants who developed chronic interfering neck pain within 12-months post-injury were predicted by depressed moods and poor endurance of the cervical extensors. Although neck strength was not identified as a predictor of future neck pain in this study, the findings support the assessment of physical features related to muscle strength. One inference that could be made is that disturbances in muscle function may precede the onset of pain and may contribute to the recurrence of pain. However, this needs to be tested, and the effectiveness of neck muscle endurance training in preventing the onset of CNP in those at risk should be investigated in further studies.

6.4 The quality of evidence for this thesis

The quality of the evidence in this thesis was evaluated to draw meaningful conclusions. This has been done through the use of reporting guidelines for each study design and the utilisation of various risk-of-bias tools, which are summarised in Table 6.1.

6.4.1 Reporting guidelines for each chapter

In this thesis, four studies were conducted and reported according to the general guidelines for each study design. The PRISMA guideline (Page et al., 2021) was used in Chapter Three (Alalawi et al., 2022d) to report on the systematic review. Similarly, the STROBE guidelines (Von Elm et al., 2014) were followed when reporting observational studies in Chapters Two (Alalawi et al., 2022c), Four and Five (Alalawi et al., 2022a). The use of such reporting guidelines is likely to inform readers and reviewers of what has been investigated and discovered, as well as to improve the standard of reporting and the efficiency of the peer review process (Von Elm et al., 2014).

6.4.2 Risk of bias for each chapter

For Chapters Two and Five, the Newcastle-Ottawa Scale (NOS) was used to assess the risk of bias in observational studies within these chapters. It was considered to be a suitable instrument for such studies since it is simple to use and includes clear assessment items (Sanderson et al., 2007, Hootman et al., 2011). The maximum score for this tool is 9, which indicates a low risk of bias in methodological quality. It assesses the likelihood of bias in three areas: selection of participants, comparability of study groups, and ascertainment of outcome. The scale, however, does not have a specific criterion to evaluate the blinding of the assessor and participants, nor a criterion to indicate whether the sample size of a study is optimal. Therefore, two items, namely, ‘representativeness of the cases’ and ‘ascertainment of exposure’, were used to assess the sample size and blinding, respectively.

In both chapters, the risk of bias was rated as moderate (7/9). This was because two items were not awarded any scores. Item related to ‘representativeness of the cases’ did not get any score due to the small sample size in both chapters. Similarly, due to the lack of blinding in both chapters, the item ‘ascertainment of exposure’ scored zero as well.

In addition to NOS, the QUIPS tool was used to assess the risk of bias in the section related to longitudinal analysis in Chapter Five. Further details about this tool were reported previously in Chapter Three, section 3.3.9, page 71. Based on the overall score of this tool, the risk of bias in this chapter was judged to be moderate, due to the lack of assessor blinding and the relatively small sample size.

Due to the early nature of this study and the lack of an adequate technique to assess the risk of bias in a longitudinal correlation analysis study, the quality of the evidence from Chapter Four was not evaluated.

In Chapter Two, the quality of the systematic review was critically assessed using the AMSTAR-2 (A MeaSurement Tool to Assess systematic Reviews) (Shea et al., 2017). This is a tool designed for conducting critical appraisal of systematic reviews in healthcare intervention of randomised or non-randomised studies. The tool did not generate an overall score.

After the evaluation of our review using the tool, we adhered to almost all of the criteria of the tool. This includes a published protocol for the review, which was published *a priori* (Alalawi et al., 2019), in addition to PROSPERO registration. A thorough and systematic literature search method, providing a list of excluded studies with justifications and the use of the QUIPS risk of bias tool are additional criteria that were met. Although one item from the tool was not reported (the source of funding for the included studies), we believe this had no impact on our review, as no studies were funded by industry. Adhering to almost all the factors in the AMSTAR tool ensures that the review has not been influenced by any bias (Shea et al., 2017). Therefore, the overall quality of our review in Chapter Two is likely to be high (Shea et al., 2017).

Table 6.1: Summary of the tools and reporting guidelines used for assessing the quality of evidence of this thesis

Chapters	Study design	Reporting guidelines	ROB tool	ROB (overall rating)
Chapter Two	Case-control	STROBE	NOS	Moderate risk of bias (7/9)
Chapter Three	Systematic review	PRISMA	AMSTAR-2	There is no overall score provided by the tool.
Chapter Four	Longitudinal study	STROBE	-	-
Chapter Five	Cross-sectional	STROBE	NOS	Moderate risk of bias (7/9)
	Longitudinal study	STROBE	QUIPS tool	Moderate risk of bias (moderate)

ROB: risk of bias; STROBE: strengthening the reporting of observational studies in epidemiology; NOS: Newcastle-Ottawa Scale; AMSTAR: a measurement tool to assess systematic reviews; QUIPS: quality in prognostic studies.

6.4.3 Minimising the risk of bias within prognostic research

As summarised in section 3.4.2, page 75, the methodological quality of the studies included in Chapter Three was mostly of poor quality (Alalawi et al., 2022d). From the 14 studies included in the review, only 5 studies were judged as having a low risk of bias, while 4 and 5 studies were judged as having a moderate and high risk of bias, respectively (Alalawi et al., 2022d). Several limitations contributed to the overall poor quality, including the high attrition rate, not adjusting for important confounders, insufficient details for the statistical analysis, and/or poor reporting. Therefore, to improve the quality of studies that assess the prognostic ability of measures of physical function in patients with whiplash injury, several measures to tackle these limitations should be considered.

Several guidelines were published aiming to improve prognostic research in healthcare. This includes guidelines from the SPIRIT 2013 Statement (Chan et al., 2013), the Transparent Reporting of a Multivariable Prediction Model for Individual Prognosis Or Diagnosis (TRIPOD) statement (Collins et al., 2015), the Quality In Prognosis Studies (QUIPS) tool (Hayden et al., 2013), the CHecklist for critical Appraisal and data extraction for systematic Reviews of prediction Modelling Studies (CHARMS) (Moons et al., 2014), and the PROGRESS framework (Steyerberg et al., 2013). As prognostic research involves different study designs and phases, further details of these guidelines are out of the scope of this thesis, but researchers should explore these guidelines when designing their prognostic studies.

6.5 Overall strengths and limitations

6.5.1 Overall strengths

There are many strengths to this thesis. First, the thesis presented studies that have assessed multiple measures throughout different stages of pain following a whiplash injury, including acute, chronic and recurrent pain, which were compared to healthy controls. This enabled us to explore which features were similar, either in the presence or absence of pain. Second, the study in Chapter Two was the first to assess and indicate the presence of altered features related to dynamic movement (velocity and smoothness of movement) in people with acute WAD. The predictive ability of such measures was not assessed before, as indicated in Chapter Three, but the association of kinematic features in extension with persistent pain and disability was found in Chapter Four. Finally, another novelty of this thesis is the assessment of comprehensive measures of physical and self-reported features in people with RNP following a whiplash injury who were asymptomatic at inception, as seen in Chapter Five.

6.5.2 Overall limitations

The specific limitations of each study within this thesis are reported in each chapter. One limitation of the study in Chapter Two is that the device (G-WALK) used to collect features of cervical kinematics was designed for gait analysis. To the best of my knowledge, its psychometric properties have not been assessed for neck movement. Furthermore, the measurement error for this device has not been assessed yet. One potential source of measurement error in the G-WALK sensor is related to the calibration of the device (Thomas et al., 2022). However, this risk was minimised as the device was calibrated before each task, as reported previously in page 45. Another source of measurement error in the G-WALK sensor is the variability in the placement of the sensor on the participant's body (Thomas et al., 2022). However, the placement of the device in Chapter Two was in line with previous studies, as reported in page 45.

One of the main limitations of this thesis is the relatively small sample size of the studies. This is apparent in many chapters, including Chapters Two, Four and Five. The reason for not achieving the preplanned numbers was the COVID-19 pandemic, which resulted in severe disruption to data collection at both sites and halted data collection. However, the sample size in Chapters Two and Five was comparable to previously published studies.

On the other hand, since Chapter Four is a longitudinal analysis of Chapter Two, the small sample size is a major limitation, which has led to modifying the data analysis. Initially, the aim of Chapter Four was to investigate the predictive ability of baseline features on persistent WAD using regression analysis. However, with 15 participants (instead of 150 participants) at 6 months, it was not feasible to conduct a regression analysis, as such analysis would likely produce overfitted and misleading findings given the number of potential predictors. Consequently, an alternative and feasible analysis was used, involving a correlation analysis to assess the association between baseline features and persistent WAD. Although the type of analysis changed, the findings in the chapter are important, as they show a linear association between features of cervical kinematics in extension and persistent WAD. This sets the scene for future studies.

Finally, the small sample size in Chapter Five may have resulted in an underpowered study. Although some measurements were significantly different across the three groups, some showed a trend at the baseline, but this trend did not reach the significance level. Despite the sample size, a comprehensive assessment was employed. In this chapter, many features related to cervical movement, neuromuscular function, psychological function and quality of life were assessed. This highlights features that are worthwhile for healthcare practitioners to assess and treat and may inform future research.

Besides the small sample, another limitation of this thesis is the abandonment of some measurements related to neuromuscular function and muscle force in people with acute WAD (Chapter Two), which are summarised in Table 1.4. This would have allowed us to compare the physical and psychological features of people with acute WAD and those with RNP and CNP. However, our pilot study indicated that such measurements appeared to aggravate neck pain in people with acute WAD, given that a maximum force was required. Furthermore, several issues arose during the collection of muscle activity using EMG with the initial device available, which were summarised in section 2.3.2, page 41.

The generalisability of this thesis may be limited. This is because the degree of pain and disability in people with neck pain are associated with movement dysfunction, as seen in Chapter One. Chapter Two included participants with acute WAD who presented with a mean score of 32.8 on the NDI, indicating moderate to severe neck disability. Therefore, the findings from this chapter might not apply to people with lower neck pain disabilities. Similarly, participants with RNP in Chapter Five presented with lower NDI scores (a mean of

5.5), which may be generalisable to people with greater disability. Another risk to the generalisability of the findings in this thesis is the general adoption of a convenience sample. Finally, women represented the majority of the included participants in this thesis. However, we believe this risk is limited, as no significant differences were found between the genders in any chapter. This proportion of women to men is supported by a recent finding indicating that women are more susceptible to neck pain than men (Lee et al., 2018).

6.6 Potential clinical implications

The findings of the research covered in this thesis have immediate clinical implications that could help with the assessment and treatment of patients with WAD. Physical features related to cervical kinematics were assessed throughout this thesis at different pain stages. This thesis emphasised the significance of examining the dynamic features of movement and not only ROM. Based on the findings from Chapters Two and Four, velocity and smoothness of movement in most directions were significantly different between healthy controls and people with neck pain. In addition, such features in extension were associated with ongoing pain and disability six months post-injury. Thus, this thesis provided an initial indication of the value of using measures of velocity and smoothness to assess patients with neck pain and to distinguish them from healthy controls. In addition, it provided preliminary evidence to help clinicians understand the relevance of these features to ongoing pain and disability in people with WAD.

The significance of assessing the dynamic features of movement in clinical practice was also emphasised in Chapter Five. Significant differences were seen between people with RNP and healthy controls in velocity and smoothness of movement, but not in ROM. This provides another indication of the importance of assessing the presence of disturbed dynamic movement characteristics in people with RNP and not simply how far the neck can move.

There is evidence that suggests such measures are usually overlooked, and ROM is the only one commonly assessed (Jull, 2011). Disturbances in these features could be a target for intervention in people with RNP.

One drawback to assessing such features is the need for special equipment that may not be available in clinical settings. However, IMUs, such as the G-Walk, are small and portable devices that do not require specific training. Furthermore, alternative methods for assessing cervical kinematics exist, including the use of smartphone devices, which are widely used. Preliminary evidence for these methods has been shown to be valid and reliable in assessing cervical ROM, velocity and smoothness of movement (Elgueta-Cancino et al., 2022, Banky et al., 2019, Palsson et al., 2019). Future research should explore other clinically applicable assessment techniques that can detect changes in cervical kinematics in patients with neck pain.

In individuals with acute WAD, clinicians should be aware that features of cervical kinematics could be influenced by perceived disability and pain catastrophising but not by fear of movement.

Besides assessment, these features deserve future attention, especially concerning generating a tailored treatment and monitoring the effects of the intervention. For example, such features can be assessed in people with neck pain, and if a disturbance is detected, treatment can be provided. One advantage is that all measures explored in this thesis are modifiable and can be assessed to determine rehabilitation programmes. In addition, they may be relevant for reducing the transition to CNP, managing symptoms in those with CNP, and reducing recurrence rates in those with RNP.

The results of the longitudinal analyses in Chapter Five provided evidence that ongoing disturbed muscle strength is present in people with RNP who are pain free (Alalawi et al., 2022a). In addition, reduced neck strength in flexion predicted poor outcomes in people with RNP (Alalawi et al., 2022a). This emphasised the importance of the assessment and treatment of physical function, especially muscle strength, and did not only feature related ROM and self-reported outcomes. There was evidence showing a sustained reduction in muscle strength in people with acute WAD, which persists for up to 12 months (Kasch et al., 2001c), although movement-related function was restored (Krogh and Kasch, 2018). Therefore, restoring optimal muscle strength may reduce, prevent or limit poor outcomes. Recent research has found that strengthening programmes are more effective than usual care or no intervention in reducing neck pain in both the short and long term (Frutiger and Borotkanics, 2021, Iqbal et al., 2021).

6.7 Integration of findings with the latest clinical practice guidelines

An evidence-based clinical practice guidelines for the assessment and management of neck pain was previously published (Blanpied et al., 2017). The International Classification of Functioning, Disability, and Health framework was incorporated into the guidelines to ensure comprehensive and patient-centred care (World Health Organization, 2007). Using a biopsychosocial model of care, the published guidelines aimed to provide healthcare professionals with a structured method for diagnosing, classifying, and managing individuals with neck pain. The aim of this section is to compare the recommendations from this guideline with the findings of this thesis.

Several recommendations based on current evidence were indicated in those clinical practice guidelines (Blanpied et al., 2017). When establishing a prognosis in patients with acute WAD, clinicians should gather and take into account various factors, including pain intensity, level of self-rated disability, pain-related catastrophising, posttraumatic stress symptoms, and cold hyperalgesia. Their predictive ability is supported by moderate- to high-level evidence (Blanpied et al., 2017). This recommendation is in line with the findings of this thesis. Chapter Three of this thesis found that higher pain intensity at baseline and a higher level of disability predicted poor outcomes in people with acute WAD (Alalawi et al., 2022d). Similarly, higher pain catastrophising was associated with ongoing pain and disability six months later in individuals with WAD, as seen in Chapter Four. However, posttraumatic stress symptoms and cold hyperalgesia were not considered in this thesis.

Another recommendation was that clinicians should include assessments of impairments of body function that can establish baselines and monitor changes over time when evaluating a patient with neck pain (Blanpied et al., 2017). However, the assessment of movement was only related to static movement (i.e., ROM) and did not consider the assessment of dynamic movement. Features of dynamic movement such as velocity and smoothness of movement were found to have clinical utility in individuals with acute and chronic WAD. For example, this thesis indicated that, compared to healthy individuals, people with acute and chronic WAD had significant alterations in all features of cervical kinematics tested, including ROM, velocity, and smoothness of movement (Alalawi et al., 2022c, Alalawi et al., 2022a). In addition, these features were found to be associated with ongoing pain and disability six months later in individuals with acute WAD when performing neck extension. Yet, measures of dynamic movement have not been considered in the previous clinical guidelines (Blanpied et al., 2017). One reason for not including the assessment of such features in the clinical recommendation might be related to the lack of evidence at the time the guidelines were developed.

Neck pain is a recurrent disorder, as discussed previously in the introduction of this thesis, section 1.3.7.1, page 28. However, the current clinical practice guidelines did not provide any recommendations about the management of individuals with RNP following a whiplash injury (Blanpied et al., 2017). Chapter Five in this thesis indicated that people with RNP, even when they are pain free, presented with similar disturbances to individuals with

CNP in neuromuscular and psychological function (Alalawi et al., 2022a). In addition, it was found that reduced strength in neck flexion, in conjunction with a greater number of previous pain episodes within the last year, were predictive of greater neck disability six months later. Therefore, the integration of this preliminary evidence with future studies should be included in future clinical practice guidelines.

6.8 Future research

In light of the findings of this thesis, future research should examine the value of exercise with psychological programmes in the acute and recurrent stages to improve physical and psychological functions. The aim of rehabilitation programmes should be to address cervical kinematics and neuromuscular changes, along with modifying maladaptive beliefs. In people with acute and chronic WAD, many intervention programmes for addressing reduced cervical movement have been designed, but other physical features, such as slowed movement velocity, control or quality, have received less attention (Jull, 2011).

The findings in Chapter Two support the clinical utility of assessing movement features at baseline (Alalawi et al., 2022c), and Chapter Five also showed an association with ongoing pain and disability six months following WAD. Based on these early findings, future longitudinal studies should explore the possible predictive relevance of cervical kinematic measurements in the transition from acute to chronic WAD.

Our attempts to assess features related to neuromuscular function and force in people with acute WAD were not successful, as indicated in section 2.3.2, page 41. Therefore, the presence of such impairments soon after injury and their predictive ability should be explored in further studies. During our pilot study in Chapter Two, two issues were encountered: the assessment of muscle force aggravated pain in some patients and there was poor quality of EMG data. The former might be done differently by selecting an arbitrary neck pain threshold at which point data collection should be terminated. Additionally, some measurements, such as JPE, could be excluded from the evaluation because they did not statistically differ between the groups in this thesis. To overcome the latter problem, an EMG device with less preparation time and a more reliable signal could be used. In Chapter Five of this thesis, a different system (Ultium® EMG System, Noraxon, USA) was utilised to measure the activity of the superficial neck muscles.

The findings in Chapter Five revealed that future neck pain and disability are predicted by neuromuscular function, particularly lower neck strength (Alalawi et al., 2022a). A randomised controlled trial might be the next step to determine whether strengthening cervical muscles can reduce the recurrence rate and disability, leading to a lower recurrence rate in people with RNP following a whiplash injury.

Muscle strength and endurance were impaired in people with RNP and were similar to those with CNP (Alalawi et al., 2022a). Therefore, further exploration is needed to identify the dosage and progression of exercises in individuals with RNP and CNP to return muscle function to normal.

6.9 Conclusion

The findings of the studies summarised within this thesis are aimed at assisting healthcare professionals and researchers to understand the type of physical and psychological disturbances that arise in patients who experience acute, chronic or RNP as a result of whiplash injury. Features of cervical kinematics and psychological function were observed to be impaired shortly after a whiplash injury and persist in people with CNP and RNP, even when the latter were examined during a period of remission. In addition, preliminary research also showed a link between altered cervical movement in extension and ongoing pain and disability after a whiplash injury and that higher neck disability was predicted in patients with

RNP based on a history of prior neck pain episodes and less neck muscle strength in flexion. The findings support the notion that the evaluation of dynamic cervical movements and psychological function should be incorporated into the early clinical assessment of people with WAD, as they were mostly impaired across various pain phases and even in people who did not exhibit pain symptoms. This thesis also emphasised the need for more research into this population and the potential benefits of early intervention programmes that aim to alleviate physical and psychological features to reduce the progression to chronicity and lower recurrence rates.

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APPENDICES

Appendix 26: Participant information sheet for people with chronic neck pain

Appendix 27: Initial recruitment poster for both groups with neck pain

Appendix 28: Modified (amendments 1) recruitment poster for people with recurrent neck pain (within UoB campus)

Appendix 29: Recruitment poster (amendments 1) for people with recurrent neck pain (Facebook post)

Appendix 30: Recruitment poster (amendments 2) for people with recurrent neck pain (Facebook post)

Appendix 31: Recruitment poster (amendments 1) for people with recurrent neck pain (Local newspaper)

Appendix 32: Consent form for people with recurrent neck pain

Appendix 33: Consent form for people with chronic neck pain and healthy participants

Appendix 34: Eligibility criteria and baseline self-reported outcome measures

Appendix 35: Outcome measures for the longitudinal analysis

Appendix 36: Box plots for cervical kinematics and proprioception

Appendix 37: Box plots for joint position error

Appendix 38: Graph for coefficients paths of LASSO regression (outcome: NDI at six months)

Appendix 39: Graph for coefficients paths of LASSO regression (outcome: number of days with pain over the 12-month period)

Appendix 1: Alalawi et al. (2019)

Open access Protocol

BMJ Open

Are physical factors associated with poor prognosis following a whiplash trauma?: a protocol for a systematic review and data synthesis

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ABSTRACT

Introduction Mitigating the transition from acute to chronic whiplash-associated disorders (WAD) is fundamental, and this could be achieved through early identification of individuals at risk. Several physical factors such as angular velocity, smoothness of neck movement and coactivation of neck flexors and extensors, have been observed in patients with WAD, but their predictive ability after a whiplash injury have not been considered in previous reviews. Therefore, the aim of the current protocol is to outline the protocol for a systematic review that synthesises the current evidence of which physical factors can predict ongoing pain and disability following a whiplash trauma.

Methods and analysis Two independent reviewers will search for studies in several electronic databases including MEDLINE, Embase, CINAHL, PsycINFO, Scopus and Web of Science as well as grey literature. Observational cohort studies will be considered if they involve participants with acute WAD followed for at least 3 months post-injury. Studies will be required to assess the prognostic ability of one or more physical factors that directly involve a body function and/or structure and can be measured objectively. Further, patient-reported outcomes of physical function will be considered. The primary outcome for this review is Neck Disability Index, while all other validated measures will be considered as secondary outcomes. Risk of bias across individual studies will be assessed using the Quality In Prognostic Studies tool along with the Grades of Recommendation, Assessment, Development and Evaluation method to assess the quality of evidence. A meta-analysis will be conducted depending on homogeneity and the number of available studies. If appropriate, data will be pooled and presented as odds ratios, otherwise, a qualitative synthesis will be conducted.

Ethics and dissemination Ethical approval is not required for this systematic review. The result from this review will be published in peer-reviewed journals.

PROSPERO registration number CRD42019122559

Strengths and limitations of this study

- This systematic review will be the first to rigorously summarise and evaluate the current body of evidence regarding the predictive ability of physical factors following a whiplash trauma, using a combination of clinical and patient-reported outcome measures.
- Several methodological limitations across included studies are anticipated such as substantial heterogeneity, high risk of bias, variabilities in whiplash severity and source of participants, which may lead to potential difficulty in interpreting and applying the results.
- This review will consider studies reported in English language only and therefore may miss studies published in other languages.

INTRODUCTION

Whiplash is a term used to describe an injury mechanism associated with a sudden forward and backward movement of the head that is usually due to car collision.[1] This sudden impact may result in injuries to multiple structures in the neck,[1] which lead to the development of a wide range of clinical manifestations commonly termed as whiplash-associated disorder (WAD).[1] WAD has a substantial socioeconomic burden,[2] with costs to the UK economy ~£3 billion per year.[3] It is a source of disability[4 5] with common negative consequences including limited work ability, fatigue, restricted participation in sports, depression, frustration and anger.[6 7]

The rate of transition from acute to chronic WAD is high. It has been found that 50% of patients with acute WAD develop chronic WAD,[5 8 9] a condition that tends to be resistant to treatment with limited evidence of effective interventions.[10 11] Additionally, there is a large variability between individuals in how they respond to a specific intervention.[12] For example, only up to 44% of patients with chronic WAD reported a significant reduction in pain following a 12-week programme of specific neck exercise.[12] Due to this general lack of responsiveness to interventions, mitigating the transition to chronic WAD, in the first place, is fundamental. This could be achieved through early identification of physical factors that increase the risk of developing persistent symptoms, among whom, a better allocation of treatments could be prescribed.[13]

Many syntheses have been conducted in the field of WAD prognosis aiming to identify factors that are associated with the outcomes following a whiplash trauma. To this end, 12 systematic reviews focused on prognosis following a whiplash injury were found,[5 8 14–23] and covered a myriad factors including social, psychological and physical factors. A review of these reviews found that an initial high level of neck pain and disability following a whiplash injury is associated with poor outcome.[24 25] However, there is still inconsistency in the reported evidence concerning the predictive ability of other factors including post-injury anxiety, catastrophizing, cold hyperalgesia, legal and compensation factors, WAD grading and early healthcare use.[24] Additionally, there is inconsistency in the results among systematic reviews regarding the predictive ability of physical factors (eg, restricted cervical range of motion (ROM)).

Qualitative synthesis from systematic reviews showed limited evidence about the association between restricted cervical ROM and persistent disability,[16 21 22] whereas no such association was found in another review.[8] This was also shown in a meta-analysis of six cohorts investigating the prognostic ability of restricted ROM on persistent neck pain and disability.[19] Due to this controversy and to the fact that it has been 6 years since the last systematic review on physical factors,[16] a systematic review is needed.

Several other physical factors have been observed to be impaired in patients with WAD, yet they have not considered in current reviews. These include changes in motor function and muscle behaviour such as decreased maximum angular velocity,[26 27] larger jerk index (a measure of the smoothness of neck movement)[27] and increased coactivation of neck flexors and extensors.[28] The presence of these adaptions was also observed in experimental pain studies,[29–36] where patients injected with a hypersaline solution inducing an immediate pain similar to a traumatic event. Besides, patient-reported outcome measures to assess physical function could be useful in predicting outcomes following a whiplash trauma.

Physical functioning was recommended by an international multidisciplinary panel as one of the core domains to be reported in clinical studies involving patients with WAD,[37] and low back pain.[38–40] 'Physical function is a broad domain that can encompass various aspects of a person's life including ability to carry out daily activities, eg, household tasks, recreational activities or self-care to specific strength, endurance and functional capacity'.[37] Yet, there is no consensus on the measurement instruments of physical functioning in the field on whiplash. Recommendations on selecting measurement interments to measure physical functioning were formulated in individuals with low back pain,[40] including Oswestry Disability Index V.2.1a and 24-item Roland-Morris Disability Questionnaire.

Therefore, the aim of this systematic review is twofold: (1) To inform and summarise the objective physical measures that have been used to date in prognostic research in this population and (2) To synthesise the evidence regarding the predictive ability of these physical factors on neck pain and disability in individuals following a whiplash trauma.

METHODS AND ANALYSIS

Registration and methodology

This is a protocol for conducting a systematic review aiming to identify whether physical factors are associated with ongoing pain and disability following a whiplash trauma. The protocol was planned according to the guidelines proposed by Moons *et al* for conducting prognostic reviews,[41] and reported according to the guidelines from Preferred reporting items for systematic review and meta-analysis protocols,[42] the Cochrane Handbook[43] and the Cochrane Back Review Group guidelines.[44]

Protocol registration

The protocol of this review was registered on PROSPERO (International Prospective Register of Systematic Reviews).

ELIGIBILITY CRITERIA

Inclusion criteria

Studies

Observational studies will be included if they describe the association between physical factors and prognosis in individuals who have sustained a whiplash injury and who have been followed up over time for a minimum of 3 months. Other study designs such as case reports or case-control studies will be excluded from this review, as well as any review articles, letters, editorials, conference proceedings and studies with only abstracts. Only articles published in English will be considered.

Participants

Studies will be included if they involve populations with the characteristics below:

1. Participants with acute WAD (<6 weeks) attributed to a motor traffic collision or sports injury and classified as grade I, II or III on Quebec Task Force (QTF) classification.[1] If the cause of acute WAD was not specified, the paper will be considered as well.
2. Participants were followed up over time for at least 3 months. Studies with different time-points beyond 3 months will be considered.
3. Aged >16 years old

Exposure or intervention (potential prognostic factors)

Studies will be required to assess the prognostic ability of one or more physical factors measured at baseline regardless of the measurement used. Because there is no consensus on the definition of physical factors specifically

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in the field of WAD, physical factors will be selected, for the purpose of this review, if they directly involve a body function and/or structure and can be measured objectively. These include neck self-reported measures of physical functioning (eg, patient specific functional scale, physical component of the SF-36), joint position sense, movement sense, proprioception, onset and amplitude of muscle activation, range of neck movement, quality of neck movement, velocity of neck movement, tests of eye movement control, neck muscle strength and endurance, neck muscle fatigue, balance and the morphology of the cervical spine muscles. Any spinal structural changes or findings in X-ray will not be considered in this review.

Outcome

The primary outcome of interest is the Neck disability Index[45] measured at least at 3 months follow-up. All other validated outcomes that were used in primary studies to describe the association between physical factors and an outcome will be included in the review and considered as secondary outcomes of interest such as pain intensity, psychological status, health-related quality of life, self-rated recovery and functional recovery.

Exclusion criteria

Other study designs such as case reports or case-control studies will be excluded from this review, as well as any review articles, letters, editorials, conference proceedings and studies with only abstracts. Only articles published in English will be considered. Also, studies will be excluded if they include patients with previous cervical pain, surgery or combine subjects with WAD and other musculoskeletal injuries.

Search strategy

Several databases will be searched from 1995 to August 2019 including MEDLINE (OVID), Embase (OVID), Cumulative Index to Nursing and Allied Health Literature (CINAHL), PsycINFO (OVID), Scopus and Web of Science as well as grey literature through Zetoc database which includes any document that usually not published commercially as a peer-reviewed article.[46] The identified keywords in box 1 will be used to search for relevant studies including unpublished articles. We limit our search to 1995 as the standardised definition of WAD was provided by the QTF monograph, an approach used previously in a systematic reviews.[14 19] Notable authors in the field will be contacted to identify relevant unpublished literature which is currently in preparation. Moreover, reference lists of retrieved individual studies will be screened for relevant studies as well as any relevant published reviews on prognosis in WAD to ensure all related studies have been identified. The searching process will be limited to the English language.

A combination of free text and Medical Subject Heading (MeSH) will be used to retrieve all related studies. The related search terms related to WAD, whiplash trauma and physical prognostic factors have been informed from

Box 1 Example of searching strategy for MEDLINE (OVID) electronic database

Search terms

1. Whiplash Injuries/pa, pp, rh, th [Pathology, Physiopathology, Rehabilitation, Therapy]
2. Whiplash Injur*.mp.
3. (Whiplash or WAD).mp.
4. (Motor adj accident*).mp.
5. (Motor adj crash*).mp.
6. Neck Injuries/pa, pp, rh, th [Pathology, Physiopathology, Rehabilitation, Therapy]
7. (Neck adj2 injurie*).mp.
8. (Neck adj2 Sprain*).mp.
9. (Neck adj2 strain*).mp.
10. OR/ 1-9
11. "cervical dysfunction*".mp.
12. (Neck adj2 dysfunction*).mp
13. ('Joint adj2 sense').mp.
14. joint position error'.mp.
15. sensorimotor control.mp
16. motor control.mp.
17. motor system dysfunction.mp.
18. sensorimotor dysfunction$.mp.
19. (neck adj3 sense).mp.
20. Proprioception/ or neck sense.mp.
21. neuromuscular control.mp.
22. Muscle* activation*.mp.
23. Co?activation*.mp.
24. movement* quality.mp.
25. (quality adj movement).mp.
26. (Neck adj2 motion).mp.
27. angular velocity.mp. or Rotation/
28. Eye Movements/ or Pursuit, Smooth/ or 'movement smooth*'.mp. or Motion Perception/
29. ('neck adj3 strength').mp.
30. ('neck adj3 endurance').mp.
31. ('Deep adj3 muscle*').mp.
32. ('superficial adj3 muscle*').mp.
33. onset of activation$'.mp.
34. Somatosensory Disorders/et, pp, rh [Etiology, Physiopathology, Rehabilitation]
35. ('Smooth adj3 movement').mp.
36. ('Alter* adj3 strategy*').mp.
37. Isometric Contraction/ or Co?contraction*.mp.
38. Fatigue/ or Muscle Fatigue/ or Muscle* fatigue.mp.
39. Muscle, Skeletal/ or Adaptation, Physiological/ or Peripheral adaptation.mp.
40. Fatty infiltration*.mp. or Magnetic Resonance Imaging/
41. physical measure*
42. Self adj3 measure*
43. Patient* adj3 measure*
44. Physical adj function*
45. Patient* adj2 outcome*
46. Muscular Atrophy/ or Immobilization/ or Muscle* disuse.mp.
47. Balance.mp. or POSTURAL BALANCE/
48. Atrophy.mp. or ATROPHY/
49. OR/ 11-48
50. Validat$.mp. or Predict$.ti. or Rule$.mp. or (Predict$ and (Outcome$ or Risk$ or Model$)).mp. or ((History or Variable$ or Criteria or Scor$ or Characteristic$ or Finding$ or Factor$) and

Continued

Box 1 Continued

(Predict$ or Model$ or Decision$ or Identif$ or Prognos$)).mp. or (Decision$.mp. and ((Model$ or Clinical$).mp. or Logistic Models/)) or (Prognostic and (History or Variable$ or Criteria or Scor$ or Characteristic$ or Finding$ or Factor$ or Model$)).mp.

51. (Predict* or Predictive value of tests or Scor* or Observ* or Observer variation).mp.
52. ('Stratification' or 'ROC Curve' or 'Discrimination' or 'Discriminate' or 'c-statistic' or 'c statistic' or 'Area under the curve' or 'AUC' or 'Calibration' or 'Indices' or 'Algorithm' or 'Multivariable').mp.
53. Risk Factors/ or Predict$ factor$.mp.
54. Predict$ variable$.mp.
55. Prognos$ factor$.mp.
56. Prognos$ variable$.mp.
57. (Candidate adj3 factor*).mp.
58. Candidate predictor*.mp.
59. Prognosis/ or Progn*.mp.
60. Predic*.mp.
61. OR/ 50-60
62. 10 AND 49 AND 61

previously published reviews in prognosis following WAD trauma,[8 14–16 18 19 24] and from our scoping searches. To increase the sensitivity of retrieving all related prognosis studies, the proposed prognosis filters that identified by Geersing *et al.*[47] will be utilised in addition to other filters identified previously.[48 49] The use of relevant phrases and MeSH terms are expected to be varied between databases. A total number of hits in each database and the excluded papers with the reasons will be reported in the main review. The search will be conducted by the lead author (AA) and has been informed by subject specific expertise and the completion of scoping searches. An example search in MEDLINE (OVID) is demonstrated in box 1.

Data management

Relevant citations and abstracts will be managed using EndNote V.X9 (Clarivate Analytics) software programme during the process of storing, removing duplicates and screening processes. Relevant forms will be developed to aid the screening process. A Microsoft Excel spreadsheet will be used to store all the extracted data.

Study selection

Once duplicates have been removed, two reviewers will independently conduct searches and screen titles and abstracts of the studies against the predetermined eligibility criteria to avoid missing related studies. Full text of the studies will be retrieved if eligibility were met or in case a conclusion could not be possible to be made based on the title or abstract. In the case where multiple papers were published from the same cohort that investigated the same predictor, the original cohort will be selected and then extracted for this review, an approach was used previously in published systematic reviews.[14 19 22] The same two reviewers will screen full texts eligibility and review relevant references lists. A third reviewer (DF) will be consulted to resolve any agreement by discussion if consensus could not be reached.

Data collection process

Data will be extracted using a modified data extraction form. The form will be reviewed and finalised through a pilot test of a small number of eligible studies during the process of data extraction. Both reviewers will extract the data independently, who will then meet to check the accuracy of the extracted data. A third reviewer (DF) will mediate any disagreement in data extraction.

Data items

The data extraction items were informed by the CHecklist for critical Appraisal and data extraction for systematic Reviews of prediction Modelling Studies.[41] Although this tool was designed for reviews of primary prediction modelling studies, some domains have been selected to inform selecting data items of this review. The following data will be extracted from each study: authors and year of publication, study location, study design, participants characteristics, outcomes of interest, candidate predictors, sample size, length of follow-up, items associated with risk of bias, summary statistics and methods for statistical analysis. The corresponding author of the original studies will be contacted for clarification and missing data if required. If no response is received from a corresponding author and the inquiry affects the eligibility of the study, it will be excluded from this review.

Risk of bias

To evaluate the risk of bias of included individual studies, the Quality In Prognostic Studies tool[50] will be used. The tool was designed to assess bias in review questions related to prognostic factors[51] and showed acceptable inter-rater reliability.[50] It considers six domains when assessing bias in prognostic studies; study participation, study attrition, prognostic factor measurement, confounding measurement and account, outcome measurement and analysis and reporting.[51] Each risk of bias domain is rated as a 'high', 'moderate' or 'low' based on consensus judgement from at least two assessors.[50] To assess the overall risk of bias of individual study, a study gets overall of low risk of bias, when all six domains rated as a low risk, while study judged as having a high risk a bias if ≥1 domain assessed as a high risk of bias. Two reviewers will assess the risk of bias independently. Any disagreement will be resolved by discussion or by a third reviewer (DF) if consensus could not be reached.

Quality of evidence

The overall quality of evidence for a prognostic factor per outcome across studies will be assessed using The Grading of Recommendations, Assessment, Development and Evaluation (GRADE) approach.[52] The GRADE approach criteria was modified to be used in prognostic factor research.[53 54] The adapted GRADE for prognostic factors research includes six factors that decrease the quality of evidence including 'phase of investigation', 'study limitations', 'inconsistency', 'indirectness, imprecision', 'publication bias', while two factors increase the quality 'moderate or large effect size', 'exposure-response gradient'.[53] The *phase of investigation* GRADE domain is a district for prognostic studies phase 3 and phase 2 considered the highest quality of evidence.[53] The GRADE system will be applied to assess the overall quality of evidence of confirmed prognostic factors generated from univariate results, as used previously.[55]

Data synthesis and analysis

A quantitative synthesis will be planned depending on homogeneity between included studies. If meta-analysis is not possible, a qualitative synthesis of the results will be conducted.

Summary statistics

When outcomes are binary, they expected to be presented as OR in primary studies calculated by the logistic regression model.[56] Therefore, pooled ORs will be used to calculate the effect estimate of a prognostic ability of predictors on an outcome of interest. Since it is expected that primary studies have used different effect estimators to calculate the prognostic ability of a factor on an outcome, some statistical conversions may be required. For example, if OR and risk ratio (RR) were not provided, they could be estimated manually based on the number of events among two comparative groups.[57] In case where potential predictors or outcome are continuous variables, the mean difference or adjusted mean difference will be used to represent a summary effect.[57] If needed, the mean difference may be converted into standardised mean difference when combined.[58] If estimation from available data is unfeasible, authors will be contacted to provide data. If no response is received, the study will be excluded from the meta-analysis. All statistical conversions will be reported in the main manuscript.

Data synthesis

The results will be pooled if an association between an outcome and specific prognostic factor was presented by the same summary statistics in two or more cases. OR or RR will be summarised separately if the outcome is binary whereas continuous outcome will be combined using mean difference or standardised mean difference. When continuous variables are presented using the median instead of the mean, they will not be combined and handled as it is.[57]

Because this review includes studies with univariate and multivariate analysis, it is expected that some studies will report univariate analysis and others with multivariate analysis. In this case, only the unadjusted estimates of prognostic factors will be pooled. This is because of the confounding effect of factors within a multivariate model which could give misleading results; therefore, effect estimates from multivariate models will be summarised qualitatively.

Meta-analysis

If meta-analysis is feasible, the random-effect model (DerSimonian and Laird method) will be conducted,[58] utilising the Statistical Software Package, Review Manager V.5.3.[59]

A significant univariate association between a factor and outcome will be considered present if the reported p value is <0.05 or 95% of CIs of OR or similar statistical methods do not get below one.[8] If combined results are presented, the 95% prediction interval will be calculated.[60]

Heterogeneity

Heterogeneity of the pooled estimate will be assessed using Q statistic and the I^2 test. Statistical heterogeneity will be considered significant between studies if $p<0.1$, as this test has low power.[61] Beside the Q statistic and to measure the magnitude of heterogeneity, the I^2 test will be used which gives a score range from 0% to 100%, where scores from (0% to 30%), (30% to 50%), (50% to 70%) and (70% to 100%) indicates low, moderate, considerable and substantial heterogeneity, respectively.[58] In the case of low heterogeneity, the fixed-effect model will be used as it gives weight better than the random-effect model, otherwise, the random effect model will be used.[62] However, both tests may be affected by the number of included studies which could not detect heterogeneity in some cases. Because of this, heterogeneity will also be investigated using forest plots to see if the estimated effect overlaps with all CIs across studies. If heterogeneity is present, further exploration will be performed including subgroup analysis and sensitivity analysis.

Subgroup analysis

Subgroup analysis is planned to clarify the source of heterogeneity if present between studies. High heterogeneity among studies is more likely to be present. A priori potential sources of heterogeneity could arise from WAD grade, study design, source of participants, follow-up time.

Sensitivity analysis

Sensitivity analysis will be performed to examine the robustness of the results by including studies with only high-quality.

Reporting bias

A funnel plot will be used to examine publication bias within studies. Also, Egger's test will be used statistically to examine publication bias,[63] with statistical power set at $p<0.1$ due to the low power of this test, which shows evidence of publication bias. If it is suspected, the trim and fill method will be applied.[64]

Confirmation of prognostic factors

The overall decision of judging whether a factor is prognostic will be based on two criteria, an approach used previously.[55] First, the same factor must show statistical univariate association with an outcome in at least 75% of all included studies. Second, the effect of prognostic factors is consistently in the same direction of effect across all studies. Further, if a multivariate analysis about the prognostic ability of a factor is available, it will be used to confirm such association. These criteria would allow a quantitative and robust methodology which allows replicable results.

Patients and public involvement

The research question in this study was developed following consultations with patients. Patients will not be involved in the analysis and data collection of the systematic review.

Ethics and dissemination

No ethical approval is required for this systematic review, as there is no patient data being collected. The result of this review will be published in peer-reviewed journals and presented in national and international conferences.

Implication of results

The results obtained from this review will have implications for understanding the recovery after whiplash trauma. In particular, information on physical factors following whiplash injury will be synthesised and their predictive ability will be demonstrated, if present. This will inform future research agenda on the predictive ability of physical factors in patients with acute whiplash. Particularly, future studies could be designed to create and test screening tools to categorise patients with acute WAD into low risk and high risk of developing persistent symptoms, which will inform early intervention and management. Additionally, intervention resources could be targeted towards those with the risk of poor outcomes which could mitigate their risk of developing ongoing symptoms, informing health policy and clinical management. Although this systematic review focuses on physical measures only, the findings will be discussed with consideration of the current knowledge on which psychosocial factors can predict ongoing pain and disability following whiplash trauma.

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Contributors All authors contributed to the focus of the systematic review topic. AA is a PhD student with DF as Lead Supervisor and AG as Co-Supervisor. AA drafted the initial protocol with guidance from DF at all stages. MS and AG provided feedback on manuscript drafts and all authors approved the final version for publication. DF is guarantor.

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Appendix 2: Alalawi et al. (2020)

Open access Protocol

BMJ Open

Do measures of physical function enhance the prediction of persistent pain and disability following a whiplash injury? Protocol for a prospective observational study in Spain

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ABSTRACT

Introduction Not all factors that predict persistent pain and disability following whiplash injury are known. In particular, few physical factors, such as changes in movement and muscle behaviour, have been investigated. The aim of this study is to identify predictive factors that are associated with the development of persistent pain and disability following a whiplash injury by combining contemporary measures of physical function together with established psychological and pain-related predictive factors.

Methods and analysis A prospective observational study will recruit 150 consecutive eligible patients experiencing whiplash-related symptoms, admitted to a private physiotherapy clinic in Spain within 15 days of their whiplash injury. Poor outcome will be measured using the Neck Disability Index (NDI), defined as an NDI score of 30% or greater at 6 months post injury. Candidate predictors, including demographic characteristics, injury characteristics, pain characteristics, self-reported psychosocial factors and physical factors, will be collected at baseline (within 15 days of inception). Regression analyses will be performed to identify factors that are associated with persistent neck pain and disability over the study period.

Ethics and dissemination The project has been approved by the Ethics Committee of the province of Malaga, Spain (#30052019). The results of this study will be published in peer-reviewed journals.

Strengths and limitations of this study

- This protocol describes, a priori, the methods and analysis of identifying predictors of persistent pain and disability following a whiplash injury.
- Specific physical measures together with established self-reported measures will be captured within 15 days of inception.
- Candidate predictors are selected using a combination of best available knowledge and theory, and their applicability in clinical practice.
- Trajectories of self-reported pain and disability will be recorded over the 12-month study period.
- Physical measures will not be measured throughout the course of the study.

INTRODUCTION

The term 'whiplash' refers to an acceleration-deceleration motion of the neck, most commonly following a motor vehicle collision, that can result in tissue injury.[1] Following whiplash, individuals may develop a variety of clinical signs and symptoms, collectively termed whiplash-associated disorders (WADs).[1] Soft tissue damage has been detected in some individuals with WAD; however, this has not been linked to the progression of symptoms.[2–4] WAD is associated with a significant socioeconomic burden;[5]; the cost to the UK economy is ~£3 billion per year.[6] This burden is primarily acquired by those developing chronic, long-term symptoms and half of those with WAD continue to report neck pain at least 1 year after the injury.[7] This highlights the importance of early identification (ID) of features associated with ongoing pain and disability; this would facilitate personalised treatment approaches to mitigate the risk associated with the development of chronic WAD.[8]

High-quality evidence has shown higher pain and disability immediately post injury to be the most consistent factor predicting longer-term pain and disability.[9 10] Studies have examined other factors that might predict the development of ongoing pain following whiplash covering all three elements of the biopsychosocial model: demographic factors,[7 11–14] pre-existing comorbidities,[11 13 14] collision factors,[7 11–13 15–18] physical factors,[14 19–24] radiological changes,[2 25–30] societal factors[31] and psychological factors.[7 32 33] Yet, there is controversial evidence concerning the predictive ability of other factors including: general psychological distress, depression, previous neck pain, gender and the use of a seatbelt at the time of the collision.[9 14 32 34 35] This illustrates an incomplete picture regarding the predictive factors for recovery versus ongoing pain in WAD.

There has been little investigation of the predictive utility of physical factors following whiplash injury; of the studies conducted, measures of physical function have been limited to measures such as range of motion[19 20 36 37] and craniocervical flexion test performance.[38 39] Yet, physical factors may offer potential to improve prediction accuracy. For example, there is a wealth of evidence describing changes in movement and muscle behaviour.[40–42] Decreased maximum angular velocity of neck movements has been observed in individuals with chronic WAD when compared with healthy individuals.[40] Such changes in movement behaviour have been confirmed in individuals with WAD and insidious neck pain, where lower peak velocity was observed in both groups.[41] In addition, a significantly larger Jerk Index (measure of the smoothness of neck movement) has been reported in individuals with chronic neck pain of both insidious and traumatic onset, when compared with asymptomatic individuals.[41] Another feature reported in those with chronic neck pain is increased coactivation of the neck flexors and extensors,[42] which is associated with reduced neck strength.[42] These additional features have not been investigated in individuals with acute WAD, but results from experimental pain studies suggest these adaptations occur soon after pain onset and may, therefore, have relevance for ongoing symptoms in individuals with chronic WAD.[43–50]

A number of methodological limitations of previously published studies in the field of WAD prognosis have been identified. For instance, a review conducted by Walton *et al*[10] found that many predictors have conflicting results.[11 12 32] Inconsistent outcome measures have previously been used by to define recovery in WAD,[51] with a different definition of recovery used in each study.[7 52] Other reasons for inconsistency can be attributed to poor reporting[11 53] and the inclusion of subjects from different settings and at different inception points. Another recent review found controversial evidence with regards to which demographic factors, prior pain and psychological factors are associated with the transition to chronic WAD.[9]

Collectively, these limitations impact on our understanding of factors associated with the transition to chronic WAD following a whiplash injury and highlight the need for an adequately powered, methodologically robust observational study to provide useful predictive estimates. Such knowledge could lead to the development of a new clinical care pathway that matches early interventions to risk factors for poor recovery.

Aims of study

The aim of the study is to identify factors soon after a whiplash injury that predict the occurrence of persistent pain and disability 6 months later. We will include a broad range of candidate predictors, including measures of physical function with self-reported measures of pain, disability and established psychological constructs.

METHODS

Study design

The study will be a prospective observational design. This protocol has been developed in accordance with guidelines from the Standard Protocol Items: Recommendations for Interventional Trials (SPIRIT) 2013 statement,[54] the Transparent Reporting of a Multivariable Prediction Model for Individual Prognosis Or Diagnosis (TRIPOD) statement,[55] the Quality In Prognosis Studies (QUIPS) tool,[56] the CHecklist for critical Appraisal and data extraction for systematic Reviews of prediction Modelling Studies (CHARMS)[57] and the PROGnosis RESearch Strategy (PROGRESS) framework.[58]

Participants

We aim to recruit 150 individuals presenting to a private physiotherapy clinic in Malaga, Spain, with symptoms attributed to a recent (within the previous 15 days) whiplash injury. Consecutive eligible individuals will be invited to participate in the study for a follow-up period of 12 months until this target is achieved. Study recruitment will commence on November 2019 and will be completed by November 2020.

Eligibility criteria

Inclusion criteria: Adults aged 18 years or older, who are experiencing acute neck pain with or without other whiplash-related symptoms such as headache, upper limb symptoms or dizziness[59] following a whiplash injury, attributed to a recent (previous 15 days) motor vehicle collision or sports injury. An ability to understand written and verbal Spanish language is also necessary.

Exclusion criteria: Individuals who experienced cervical spine fractures or dislocations during or since their whiplash injury (WAD grade IV),[1] loss of consciousness during or since their whiplash injury[60] or have ever received neck surgery[61] will be excluded from participation. Individuals with malignant spinal disorders, mental disorders[62 63] or regular use of analgesic medication prior to the injury due to chronic pain will also be excluded.

Recruitment

Participants will be recruited from a single private physiotherapy clinic in Malaga, Spain. Based on feasibility data (clinical records), we estimate that at least 300 eligible individuals will be eligible for recruitment over a 12-month period, and that at least 50% can be expected to consent to participation.

We will recruit eligible patients within 15 days of their whiplash injury. One designated physiotherapist working at the physiotherapy clinic will manually check electronic clinical records of all consecutive patients attending the clinic. Once an eligible patient is identified at the clinic, the designated clinic physiotherapist will contact the patient to invite them to participate in the study; this invitation will be done either in-person at the clinic after the first treatment session or via telephone after patients have returned home from their clinic appointment. A verbal and written description of the study will be provided during the invitation. Those patients interested in participation will be invited to attend an initial study session at the physiotherapy clinic. At this session, the researcher will again explain the study design and context, patients will be given a detailed information sheet and written informed consent will be sought. The English version of the consent form is provided in the online supplemental file. Once recruited, participants (figure 1) will be asked to complete a baseline self-reported questionnaire, after which physical data will be collected (table 1). Participants will be informed that they can withdraw from the study at any time, without having to provide a reason. They will also be advised to carry on with their daily routines as usual, and that any interventions received during their physiotherapy sessions will be recorded for a descriptive analysis.

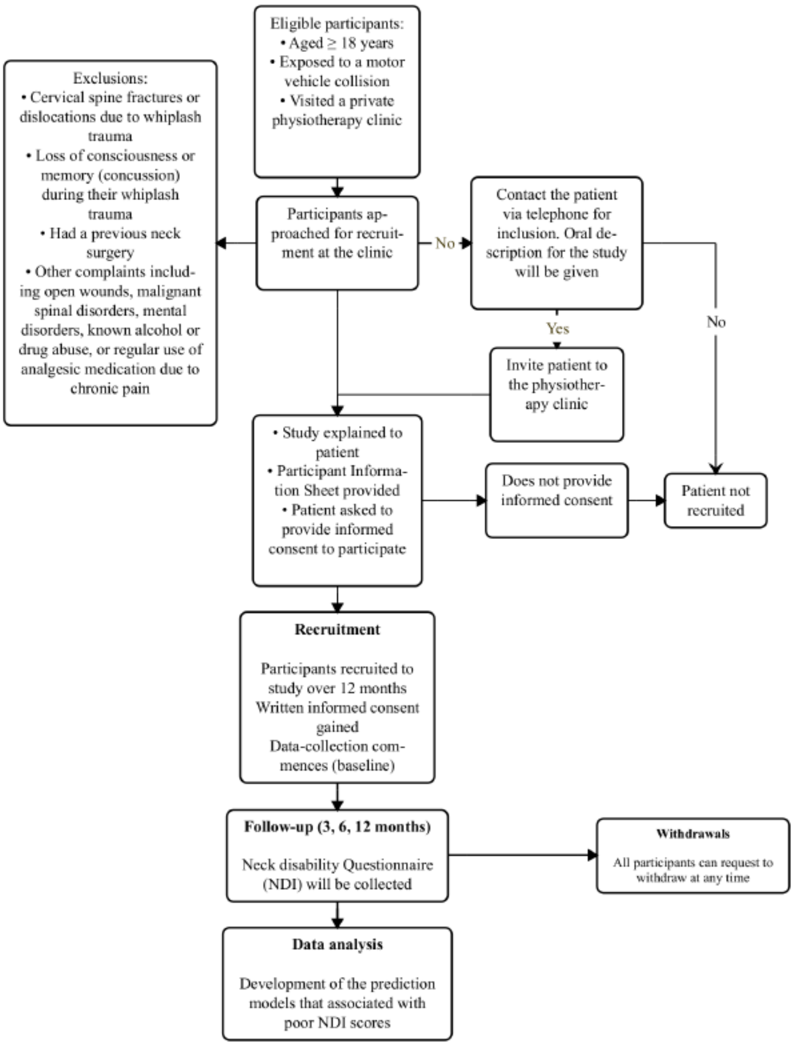

Figure 1 Participant flow through the study.

Table 1 Summary of self-reported and physical measures that will be collected

Domain/candidate predictor	Data collection instrument	Baseline commencing ≤15 days post injury	3–12 months, clinical course; 6 months, outcome assessment point
General patient characteristics including previous musculoskeletal pain			
Gender at birth	Male/female	✓	
Education	Highest educational level attained	✓	
Psychosocial features			
Catastrophising	Pain Catastrophizing Scale	✓	
Kinesiophobia	Tampa Scale of Kinesiophobia	✓	
Recovery expectation	Numeric Rating scales (NRSs)	✓	
Injury characteristics			
Disability	Neck Disability Index	✓	✓
Pain characteristics			
Current neck pain intensity	NRSs	✓	
Neck pain intensity at the end of neck range of motion tasks	NRSs	✓	
Neck pain intensity at the end of maximum contraction tasks of craniocervical flexion, neck flexion and neck extension	NRSs	✓	
Neck pain intensity at the end of submaximum contraction tasks of craniocervical flexion, neck flexion and neck extension	NRSs	✓	
Physical measures			
Neck range of motion	G-Walk (flexion, extension, rotation and side flexion)	✓	
Neck angular velocity	G-Walk (flexion, extension, rotation and side flexion)	✓	
Smoothness of neck movement	G-Walk (flexion, extension, rotation and side flexion)	✓	
Neck proprioception	G-Walk (rotation with eyes closed)	✓	
Maximal and submaximal isometric contractions	Dynamometer–evaluation of craniocervical flexion, flexion, and extension maximum voluntary contraction and control of submaximal force	✓	
Coactivation of the sternocleidomastoid and splenius capitis	Surface electromyography during physical tests described above	✓	

Outcome

Outcome will be measured using the Neck Disability Index (NDI);[64] a neck-specific self-reported questionnaire used to assess neck pain-related disability. The NDI consists of 10 items of daily activities including personal care, lifting, reading, work, driving, sleeping and recreation.[64] Each item has five ordinal response options from 0 (no disability) to 5 (complete disability), producing a maximum total score of 50, which can be expressed as a percentage (0%–100%). The reliability of NDI and validity have been established in individuals with neck pain disorders.[65]

Outcome will be assessed at 6 months for the prediction model.[66] Using 6 months as a cut-off for identifying outcome is supported by the finding that most individuals recover within 3 months of the whiplash injury, with fewer recovering after this,[11 67] and a plateau after 6 months.[68] To investigate the course of neck pain and disability, the NDI scores will additionally be collected at 3 and 6 months.

Candidate predictors

Due to the current lack of consensus on predictive factors of poor outcome, several self-reported and physical measures will be collected.[9] Factors have been selected based on current knowledge of prognosis in whiplash[2 7 9 11–13 24 31–34 69] and a theoretical association with prognosis in individuals with neck pain, as informed by the biopsychosocial model of pain.[70] These factors are also chosen due to being feasible to measure in clinical

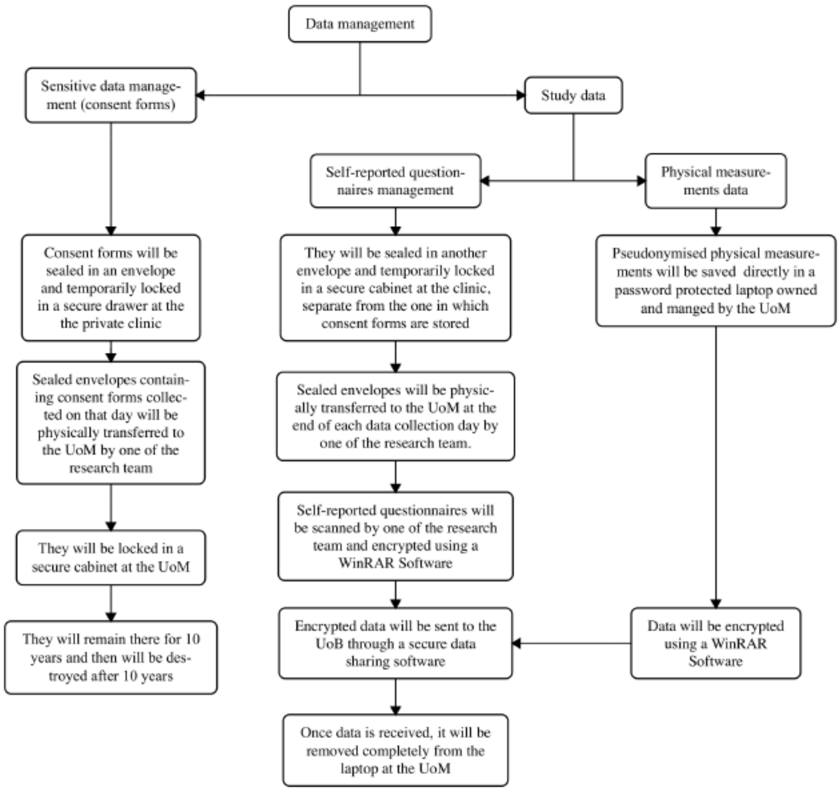

Figure 2 Process for data management. UoM, University of Malaga; UoB, University of Birmingham.

practice. Candidate predictors are summarised in table 1 with further information available in the online supplemental file S1. All data collection will be standardised through protocols and clinical report forms

Data collection

Baseline and follow-up

Baseline data including self-reported questionnaires and physical assessments will be collected immediately following recruitment, at the physiotherapy clinic, by a trained assessor within 15 days of injury. Participants will be contacted by the same assessor by telephone at the University of Malaga (UoM) at 3, 6 and 12 months follow-up, in order to complete the NDI, as used previously.[71]

Data management

Participant data privacy will be maintained throughout data handling (collection transfer, storage and processing) and will comply with data protection requirements as set out by the General Data Protection Regulation of the European Union and UK Data Protection Act 2018 (figure 2). Participant data will be tracked using only study ID numbers. Study ID numbers will be kept separate from study research data, which will be accessible only by members of the UoM research team.

Sensitive data management

Some participant data will be sensitive in nature; in particular consent forms which contain identifiable data, name, phone, contact address and study ID numbers. Once each participant has completed a consent form in the clinic, it will then be sealed in an envelope and temporarily locked in a secure drawer at the physiotherapy clinic, with access only available to members of the UoM research team. Once daily data collection has ended, all sealed envelopes containing consent forms collected on that day will be physically transferred to the UoM by one of the research team and locked in a secure filing cabinet there. Identifiable data will be securely stored at UoM for a period of 10 years, after which they will be destroyed. No identifiable data will be transferred outside of the UoM.

Self-reported questionnaires management

Self-reported paper questionnaires, identifiable only by study ID number for each participant, will be sealed in another envelope and temporarily locked in a secure cabinet at the clinic, separate from the one in which consent forms are stored. Sealed envelopes containing the pseudonymised self-reported questionnaires will be physically transferred to the UoM at the end of each data collection day by one of the research team. Once transferred, self-reported questionnaires will be scanned by one of the research team and saved in a password protected laptop computer, owned and managed by UoM. Scanned self-reported electronic data will be encrypted using a WinRAR Software before transit to the University of Birmingham (UoB) (via Power Folder data sharing software, hosted locally at the University). Once received, this pseudonymised data will be uploaded directly to physically secure servers at the UoB, where they will remain indefinitely on secure UoB servers with access restricted to members of the study team. Once uploaded to UoB servers, data will be removed completely from the laptop at UoM. The same procedures will be followed for follow-up NDI data at 3, 6 and 12 months.

Physical data management

Pseudonymised physical data will be saved in a password protected laptop owned and managed by UoM, while at the clinic study session. Access to the UoM laptop is restricted and only available to the local research team. As with other data, pseudonymised electronic data will be encrypted using a WinRAR Software, transferred to the UoB team, and uploaded to the physically secure servers at UoB, where they will remain indefinitely with access restricted to study researchers. Again, once data have been received by the team at UoB, they will be removed from UoM computers.

Data analysis

Numbers of individuals will be recorded that are: potentially eligible, examined for eligibility, confirmed eligible, recruited into the study, completing follow-up and analysed. Loss to follow-up and withdrawals will be reported, with reasons where available. Descriptive analyses of participants at baseline will include participant demographics, self-reported questionnaires and physical assessment data.

Linear and logistic regression analysis

Linear regression analysis will be used as the primary analysis to develop a linear model to determine the association between candidate predictors and neck pain and disability (measured by NDI) at 6 months post injury. Linear regression analysis was included as a primary analysis to allow for the inclusion of the outcome (NDI) without dichotomisation. This approach follows the recommendations by PROGRESS series recommending of analysing continuous variables on their continuous scale,[72] as well as to the fact that this approach method increases the statistical power and reduces information loss.

In addition to the linear regression analysis, logistic regression will be included as a secondary analysis to identify factors that are associated with poor outcomes. Outcome (NDI) scores will be dichotomised into good or poor categories with a NDI score of ≥30% at 6 months post injury defined as poor outcome, as described previously.

Variable selection

Penalisation (shrinkage) approach will be used to avoid overfitting the final prognostic model, given the minimum number of events[10] per variable will be adopted in this study to develop prognostic modes.[73]

First a full model will be constructed including all baseline candidate predictors (table 1) with their estimated adjusted regression coefficients calculated by standard methods. Next, a shrinkage method, a least absolute shrinkage and selection operator (LASSO) regression, will be used to effectively exclude candidate predictors from the final model by shrinking their coefficients to exactly zero.[74] Candidate predictors with zero coefficients will be excluded from the model, leaving the remaining candidate predictors with regression confidents of more than zero. This approach is in line with the current recommendations for variable selection in prognostic models to address overfitting.[75] Moreover, this approach is preferred when a model with fewer predictors is desired without affecting the predictive ability of the model, making it more applicable in clinical practice.[73]

Model performance

The predictive performance of the prognostic screening tool will be assessed using the established traditional measures of overall prognosis, discrimination and calibration.[76] Brier score will be used to quantify the overall performance of the screening tool where the score ranges from 0 ('perfect model') to 0.25 ('not informative model').[76] The receiver operator characteristic curve will be used to discriminate between those who did or did not develop chronic whiplash. Finally, the calibration will be assessed through plotting the mean predicted against observed chronic whiplash cases.

Sample size

This study will consider the association between 16 candidate predictors (table 1) and neck pain and disability at 6 months. The authors will ensure that at least ten participants per predictor will be used to develop an adequately powered linear regression analysis.[77 78] Because the shrinkage method by LASSO method creates models with fewer predictors,[73] it is anticipated that the number of final predictors retained in the final linear model will fall below 12 predictors. Therefore, a sample size target of 120 participants is required to adequately powered a maximum of 12 candidate predictors into the multiple linear regression, with the addition of 30 participants to allow for possible loss of follow-up (total=150).

For the sample size of a logistic regression model derived following the LASSO shrinkage method, a minimum of

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5 events per predictor is sufficient as established previously.[73] Based on the current knowledge about the transition rate from acute to chronic WAD, it is expected that 50% of patients will report persistent neck pain and disability.[11 17 79] This leaves 60 out of our potential participants who might develop persistent neck pain and disability 6 months post WAD. Therefore, a sample size of 60 participants is adequate to power a logistic regression analysis of 12 candidate predictors with 5 events per predictor.

Management of missing data

For each variable of interest, numbers of participants with missing data will be reported. Any potential bias due to loss of follow-up will be assessed and compared using baseline data of subjects who withdraw or lost at follow-up.[66] Multiple imputation[80] will be used to deal with missing outcome data, if appropriate and necessary. Participants will be excluded from the predictive model and subsequent analyses if they request to withdraw from the study following recruitment.[66]

Patients and public involvement

The research question in this study was developed following consultations with patients. Patients will not be involved in the analysis and data collection of study. The results of the study will be presented to members of the public and patients during one of our regular Patient and public involvement meetings.

Ethics and dissemination

The study will be conducted according to the Declaration of Helsinki. The project has been approved by the ethics committee of the province of Malaga, Spain, (#30052019). The results of the study will be disseminated via reports published in peer-reviewed journals and national and international conferences. No datasets will be created as part of this work for deposition or curation. Participant burden has been taken into consideration when developing this study. The number of measures has been kept to a minimum. To ensure the privacy of each patient, a unique ID number will be assigned to each participant at the time of recruitment. Only pseudonymised or anonymised data will be used during analyses. Participants will be informed that they can withdraw from the study at any time, without having to provide a reason; however, where a reason is given, it will be recorded. If a participant withdraws, no further data will be collected but data already collected will be retained for analyses. Baseline characteristics of any participants that withdraw will be compared with retained participants to assess for any differences.

At each data collection session, confirmation to proceed will be gained before any data are collected. Any concerns and/or adverse events will be noted and fed back to clinical staff, according to the good clinical practice principles. For ethical reasons, routine treatment will not be withheld from individuals at any point during the study. The details and frequency of any received treatment will be recorded and reported. The protocol and conduct of this study are strengthened by the inclusion of patient and public involvement, who contributed to the development of study design and documentation. In addition, they will contribute to the processes of performing data analysis, interpretation of results and producing a lay summary of findings.

DISCUSSION

This is the first protocol to describe, a priori, the methods and analysis for identifying predictive factors for ongoing pain and disability following acute whiplash injury. In particular, self-reported measures together with novel physical measure will be incorporated including angular velocity, smoothness of movements, force steadiness and neck muscle coactivation to predict poor outcome in individuals with WAD recruited within 15 days of the injury. The selected candidate predictors are included based on current knowledge and the possible utilisation in clinical practice. The knowledge gained through this study can assist in the ID of personalised interventions to facilitate recovery and therefore minimise the transition to chronic whiplash.

SPIRIT 2013 statement, TRIPOD, PROGRESS, QUIPS and CHARMS statements and frameworks have informed design to ensure rigorous conduct of this study.[54–58] The results from this study will provide new insights into who is likely to recover versus who is likely to develop persistent symptoms following a whiplash injury. Using a novel combination of outcome measures will allow the future development of a tool to predict development of chronic and disabling pain following a whiplash injury providing new opportunities to identify precision intervention.

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Contributors All authors contributed to the focus of this study. AA is a PhD student with DF as Lead Supervisor and AG as Co-Supervisor. AA drafted the initial protocol with guidance from DF and DE at all stages. AL-S and MF-S will be involved in collecting data from participants. All authors approved the final version for publication. DF is guarantor.

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Correction: *Do measures of physical function enhance the prediction of persistent pain and disability following a whiplash injury? Protocol for a prospective observational study in Spain*

Alalawi A, Luque-Suarez A, Fernandez-Sanchez M, *et al.* Do measures of physical function enhance the prediction of persistent pain and disability following a whiplash injury? Protocol for a prospective observational study in Spain. *BMJ Open* 2020;**10**:e035736. doi: 10.1136/bmjopen-2019-035736

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Supplementary file 1. Candidate predictors

General patient characteristics including previous musculoskeletal pain

Participants' demographic data will be recorded at baseline including gender and highest attained education level.

Psychosocial features

Pain Catastrophizing Scale (PCS)

The PCS will be used to evaluate the extent to which patients ruminate, magnify or feel helpless about controlling their pain [1]. It is a 13-item self-reported outcome consisting of three dimensions including rumination, magnification and helplessness to measure pain related catastrophizing. Subjects rate the frequency of experiencing catastrophic thoughts as 0 (not at all) or 4 (all the times) which produces an overall score of from 0-52 with higher scores indicating greater negative pain thoughts. The reliability and validity of the PCS have been established [1], and it has been used in patients with WAD [2, 3]. Moderate evidence of significant association shows that initial catastrophising was a risk factor for developing persistent symptoms in whiplash [4] with pooled odd ratio=3.77 (95% confidence intervals = 1.33 - 10.74) [5].

Tampa Scale of Kinesiophobia [TSK-11]

The TSK-11 is a self-reported outcome used to evaluate fear of movement or injury during activities [6]. It consists of 11-item of which each is scored from 1 ('totally agree') to 4 ('totally disagree') producing a total score from 11 to 44, with higher scores indicating higher fear of movement. The TSK-11 has showed excellent test-retest reliability and good construct validity in detecting changed in pain and disability [7]. Indirect association was found between fear of movement and higher neck pain and disability in patients with acute

WAD [8]; catastrophizing increases fear of movement which leads to decreased functional self-efficacy that results in higher pain and disability [8].

Recovery Expectation (high or low expectation of recovery)

Patients will be asked if they expect to fully recover within the next six months. Recovery expectations will be assessed by the question "In your opinion, how likely is it that you will be fully recovered with no persistent sequelae?" [9]. In response to this question, recovery expectations will be measured using NRS where a patient need to indicate how likely he/she would have completely recovered, by choosing a score from 0 ("not likely") to 10 ("very likely") [10]. Low expectation of making full recovery were found to be an independent predictive factor associated (odds ratio= 4.2 [95% CI = 2.1 - 8.5]) with higher disability in individuals with acute WAD [10].

Pain characteristics

Numeric Rating Scale (NRS)

Current neck pain intensity will be measured using NRS which is a 11-point scale range from 0 (no pain) to 10 (worst possible pain). Also, perceived pain intensity will be measured at the end of each physical measure of neck range of motion tasks, neck maximum contraction tasks, and neck submaximum contraction tasks. The reliability of NRS has been established in patients with neck pain (ICC:0.76) [11]. Also, participants will be asked remotely (through the app) where they have 'experienced pain during the last week' from several body locations [12]. Based on their response of chosen areas, pain intensity will be assessed using NRS. Finally, neck pain intensity following active movements will be measured through NRS. High evidence of significant association shows that initial neck pain intensity was a consistent risk factor for developing persistent symptoms in whiplash [4] with pooled odd ratio= 5.61 (95% CI = 3.74 - 8.43) [13].

Physical measures

Wearable sensor for motion detection (Neck range of movement, angular velocity, movement smoothness and proprioception)

A wearable BTS G-WALK® sensor system (BTS Bioengineering, Italy) will be utilised to assess neck range of motion, angular velocity, movement smoothness, and neck proprioception. The sensor connects to a computer via Bluetooth; at the end of each analysis an automatic report containing all the parameters recorded during the test, is displayed.

Active neck flexion, side-flexion, extension, and rotation will be measured at baseline. Impaired range of motion has been found in individuals with WAD compared to healthy controls [14, 15] and has also been found to be a factor associated with persistent disability at one year [16, 17], and neck pain and disability at 6 months [18, 19].

Besides range of motion, the angular velocity and movement smoothness will be recorded simultaneously during each neck movement. Each movement direction will be repeated five times and the average taken. These kinematic variables may provide more information about motor control disturbances [20]. A study found maximum angular velocity and acceleration were lower in subjects with chronic WAD when compared to healthy control [20]. The same finding (lower peak velocity) was found in cohorts of both WAD and insidious neck pain [21]. Moreover, significant differences in jerk indices were observed during active neck movements in a study comparing healthy controls to those with chronic neck pain of both insidious onset and traumatic onset [21].

Neck proprioception will be measured by calculating the Joint Position Error (JPE) following active neck rotation. JPE is defined as the ability to relocate the natural head position without the assistance of vision [22]. To assess this, the same wearable sensor (G-Walk) will be used. Patients will repeat active neck rotation with their eyes closed and will indicate when they think that they have returned to the starting position. JPE will be assessed three times for both right and left rotation and the average taken for each direction. Decreased head repositioning accuracy has been observed in people with idiopathic neck pain [23], but with greater repositioning errors found in individuals with neck pain attributed to a trauma [24], which is even more evident in those with moderate to severe pain and disability [14].

Dynamometer (maximal and sub-maximal isometric contractions)

At baseline, the participants will perform maximal and sub-maximal isometric contractions to measure maximum strength and control of sub-maximal forces. Cranio-cervical flexion, neck flexion and extension will be tested using a hand-held dynamometer for neck muscle testing (NOD, OT Bioeletronica, Italy).

1. Maximum voluntary contraction (MVC):

   Two MVCs will be performed for cranio-cervical flexion, neck flexion, and extension. Each maximum MVCs will last for 3 seconds, separated by 1 minute rest in between [25]. The mean MVC for each direction will be calculated and used in the analysis [26, 27]. Patients will perform an initial trial to familiarise themselves with each movement under the guidance of a trained examiner with minimal force.

   Cranio-cervical flexion strength testing will be performed with the participant in supine lying with the hip and knees flexed to approximately 90 degrees [28]. The head will be placed in neutral position and the dynamometer placed behind the upper cervical spine with the instruction being to nod as if saying yes but as hard as you can. Patients will be seated to measure neck flexion and extension strength with the participant seated comfortably on a chair with hip and knee flexed to 90 degrees with head in neutral position and feet flat on the ground. To measure neck flexion, the dynamometer will be placed over the forehead and against the resistance of the examiner, the patient will be instructed to "push as hard as you can as you try to bring your chin to your chest" [29]. The dynamometer will then be placed on the back of the head and the patient instructed to "push as hard as you can into the dynamometer as if trying to bring the back of the head to your neck" [29].

Patients with neck pain commonly present with reduced neck strength [29-32], although the extent of impaired strength is highly variable across patients [33]. Significant lower isometric MVC force has been observed in patients with chronic WAD compared to healthy controls [29]. Reduced neck muscle strength has been associated with the extent of disability [25, 34] and pain [34] in people with chronic neck pain..

2. Sub-maximal voluntary contractions:

In the same positions described for the MVC, participants will be instructed to perform a single submaximal contraction at 20% of their maximal force and hold this for 10 seconds for cranio-cervical flexion, flexion and extension. In addition, participants will perform 40%, 60%, 80%, and 100% of their maximal force for the cranio-cervical flexion only. Feedback on force will guide the participant to maintain specific degree of contraction from their MVC over the duration of the contraction.

Surface electromyography (EMG) (co-activation of the sternocleidomastoid and splenius capitis)

The amplitude of sternocleidomastoid (SCM) activity will be measured bilaterally during the isometric maximum and submaximal voluntary contractions of cranio-cervical flexion. In addition, both SCM and splenius capitis (SC) activity will be measured bilaterally during the maximum and submaximal voluntary contractions of neck flexion and extension.

Increased co-activation of the neck flexors and extensors has been observed in patients with chronic neck pain and headache [35], and is associated with reduced neck strength [35]. Changes in neck muscle activation has been observed in people with acute neck pain following a whiplash injury [14, 36].

Following gentle skin preparation, pairs of bipolar surface electrodes will be placed over SCM and SC bilaterally following published guidelines for electrode placement [37]. Signals will be detected using wireless EMG (Ultium® EMG, Noraxon, USA). Co-activation indexes will be calculated as described previously [38].

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Appendix 3: Alalawi et al. (2022a)

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Article

Assessment of Neuromuscular and Psychological Function in People with Recurrent Neck Pain during a Period of Remission: Cross-Sectional and Longitudinal Analyses

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Abstract: The aim of this study was to examine for the presence of differences in neuromuscular and psychological function in individuals with recurrent neck pain (RNP) or chronic neck pain (CNP) following a whiplash trauma compared to healthy controls. A secondary aim was to examine whether neuromuscular characteristics together with psychological features in people with RNP were predictive of future painful episodes. Multiple features were assessed including neck disability, kinesiophobia, quality of life, cervical kinematics, proprioception, activity of superficial neck flexor muscles, maximum neck flexion and extension strength, and perceived exertion during submaximal contractions. Overall, those with RNP (n = 22) and CNP (n = 8) presented with higher neck disability, greater kinesiophobia, lower quality of life, slower and irregular neck movements, and less neck strength compared to controls (n = 15). Prediction analysis in the RNP group revealed that a higher number of previous pain episodes within the last 12 months along with lower neck flexion strength were predictors of higher neck disability at a 6-month follow-up. This preliminary study shows that participants with RNP presented with some degree of altered neuromuscular features and poorer psychological function with respect to healthy controls and these features were similar to those with CNP. Neck flexor weakness was predictive of future neck disability.

Keywords: whiplash; chronic neck pain; recurrent neck pain; cervical kinematics; neuromuscular function

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1. Introduction

A whiplash injury commonly results in ongoing pain and disability, reduced work capacity, fatigue, restricted involvement in sports, depression, frustration, and anger [1–4]. The term 'whiplash associated disorder' (WAD) describes this multitude of clinical manifestations that commonly occur following the injury [5]. Over the last 30 years, the number of patients presenting to hospitals with traffic-related whiplash injuries has increased globally [6], placing a significant burden on health care and insurance systems [7–9]. Chronic neck pain (CNP) refers to persistent pain which lasts more than three months [10], while recurrent neck pain (RNP) refers to neck pain that has occurred frequently with complete pain-free periods in between. [11]. Both are common following the first episode of neck pain.

Altered neuromuscular function is a common feature in patients with acute and CNP including those that have sustained a whiplash injury [12–14]. These changes include disturbances in muscle strength, muscle behaviour and proprioception [15–18]. Additionally, restricted neck range of motion (RoM), as a static measure of movement, has been extensively documented for patients with neck pain of both traumatic and idiopathic origin [19,20]. Measures of dynamic motion such as slower [19–22], and irregular neck movement [20–23], have also been observed in people with CNP, and are associated with kinesiophobia [24]. Earlier work suggested that some measures of neuromuscular function may not always return to values seen in asymptomatic people even when pain resolves [25,26].

Several original studies and systematic reviews have aimed to identify prognostic factors associated with poor outcomes following a whiplash injury [27–29]. High-quality evidence has shown that higher pain and disability post-injury in the acute phase, are the most consistent at predicting longer-term pain and disability [30,31]. However, the predictive ability of wide range of neuromuscular adaptations has not been conducted previously. Additionally, there is very limited evidence examining the presence of neuromuscular adaptations in patients with RNP when they are pain free, i.e., in a period of remission. A recent systematic review [32], aiming to determine whether neuromuscular adaptations exist in people with recurrent spinal pain found very low level evidence to support muscle activity changes in people with recurrent low back pain, especially greater co-contraction, redistribution of muscle activity, and delayed postural control of deeper trunk muscles. Reduced range of motion of the lumbar spine was also found. Meaningful conclusions on people with RNP could not be drawn since only one study was identified [33]. In that particular study, thirty people with recurrent episodes of neck pain of non-traumatic origin were included and neck proprioception and performance on the craniocervical flexion test (i.e., the maximum pressure maintained for 10 s) were examined [33]. Both measures were able to differentiate between people with RNP and asymptomatic controls (areas under the curve of 0.69 and 0.73, respectively). However, it should be noted that the participants with RNP were not entirely asymptomatic as they presented with mild neck pain (mean scores on numerical rating scale 3.13 $\pm$ 2.01) and disability (mean scores on the Neck Disability Index 10.7 $\pm$ 5.12).

Currently there is very limited evidence on whether people with RNP who are in complete remission from their neck pain continue to display changes in neuromuscular function or psychological features such as high levels of kinesiophobia which may impact on neuromuscular function. Additionally, the predictive ability of these features in people with RNP has not been previously investigated in people who have sustained a whiplash injury. Yet this is highly relevant since the identification of physical and psychological factors that may increase the risk of developing future episodes of neck pain would provide more specific direction for appropriate treatment for the prevention of repeated episodes of pain [34,35].

The first objective of this study was to determine whether neuromuscular function and selected psychological variables are altered in people with RNP following a whiplash injury when tested during a period of remission compared to healthy people and whether these factors are comparable between people with RNP and CNP. We hypothesised that people with RNP in pain remission would present with altered neuromuscular and psychological function similar to those present in people with CNP. A secondary objective was to investigate the predictive ability of a variety of neuromuscular and psychological features for the development of new pain episodes over 12 months in those with RNP. We hypothesised that a combination of neuromuscular and psychological features could predict future ongoing neck pain episodes over the 12 months of assessment.

2. Materials and Methods

2.1. Study Design

A cross-sectional observational study, followed by a longitudinal analysis for those with RNP, was conducted and is reported according to the guidelines in the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) statement [36], with the STROBE checklist available in Supplementary Table S1. The study was approved by the

Ethical Review Committee of the University of Birmingham, UK (ERN_19-0564) and was conducted in accordance with the Declaration of Helsinki.

2.2. Participants

Three groups of adult participants (≥18 years old) were included in this study consisting of people with RNP, CNP, and healthy controls. A sample size of 15 healthy controls (mean age ± SD: 31.1 ± 5.7; female: 60%), 22 participants with RNP (mean age ± SD: 31.0 ± 11.8; female: 64%), and 8 participants with CNP (mean age ± SD: 33.6 ± 8.7; female: 88%) were included in this study (Figure 1). Those with RNP and CNP had a history of neck pain initiated following a whiplash injury, due to a motor vehicle collision. Further inclusion criteria for each group are described below.

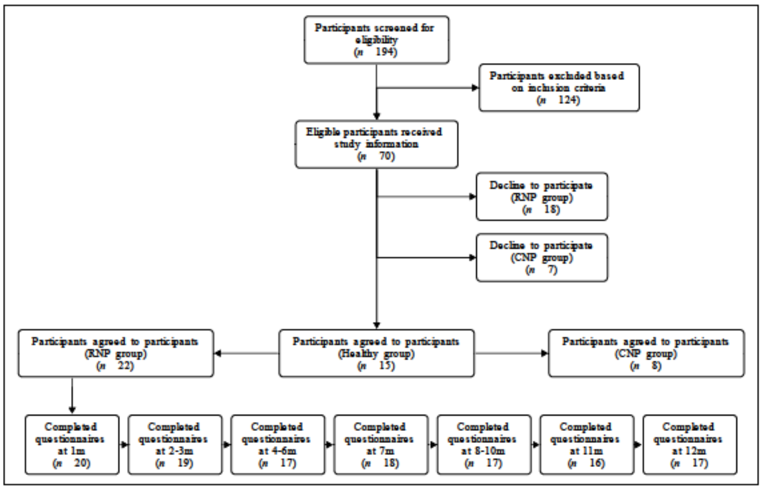

Figure 1. Flowchart of study population.

2.2.1. RNP Eligibility Criteria

Participants with RNP were included if they experienced two or more neck pain episodes (lasting ≥24 h) separated by a period of remission lasting at least 30 days during the previous 12 months, and experienced neck pain of at least 2/10 on the Numeric Rating Scale (NRS) [37] and lower than 10/50 on Neck Disability Index (NDI) [38] during an episode. These inclusion criteria are in line with the definition of recurrent low back pain [11]. Furthermore, individuals with RNP needed to be pain free at the time of assessment.

2.2.2. CNP Eligibility Criteria

Participants in this group were included if their neck pain lasted three months or more, their current neck pain was at least 2/10 on the NRS, and they scored at least 10/50 on the NDI [38].

2.2.3. Healthy Participants Eligibility Criteria

Healthy participants were required to have no current neck pain and no history of neck or shoulder pain that required treatment from a healthcare professional.

2.2.4. Exclusion Criteria of All Groups

Participants were excluded if they participated in a neck or shoulder rehabilitation programme during the past three months or had any of the following: a history of neck or shoulder surgery [39], malignant spinal disorders, rheumatic condition, mental disorders [40,41], pregnancy, or regular use of analgesic medication prior to the injury due to chronic pain.

2.3. Recruitment

All participants were recruited from the community in Birmingham, UK, including staff and students at the University of Birmingham. The study was advertised using posters, local newspaper, and social media (Facebook) to expand the reach of the study. Initially, a researcher (AA) assessed the eligibility criteria of potential participants, sent the participant information sheet to participants via email, and answered any questions via email or telephone. Once an interested and eligible participant was identified, they were invited to attend one session at the University of Birmingham where the study was explained, a hard copy of the information sheet was provided, and written informed consent was obtained. Once consent was obtained, all participants were asked to complete self-reported questionnaires and undergo physical testing which occurred on the same day.

2.4. Baseline Measures (Candidate Predictors)

Patient-Reported Outcome Measures

The number of episodes referred to the number of pain episodes (over that last 12 months) that lasted more than 24 h with at least 30 days remission. The average pain intensity during an episode was assessed using the Visual Analogue Scale (VAS) [42], ranging from zero (no pain) to 100 (worst pain imaginable). The validity and reliability of the VAS have previously been established [43–45]. Neck pain duration was calculated in months and assessed only for the participants with CNP. Current pain intensity (for the CNP group only) was assessed using VAS immediately prior to physical data collection, by asking participants to indicate their current neck pain intensity.

To assess perceived neck disability at baseline, the NDI [38] was used which consists of 10 items related to daily activities such as reading, lifting, driving, personal care, work, sleeping, and recreation [38]. Each question has five ordinal response options from 0 (no disability) to 5 (complete disability) and the NDI scores are interpreted as recovered (NDI < 8), mild pain and disability (NDI 10–28), moderate/severe pain and disability (NDI > 30) [46]. The NDI is a valid and reliable measure in individuals with neck pain disorders [47].

The Tampa Scale of Kinesiophobia (TSK-11) [48] was used to assess fear of movement or injury during activities. It consists of 11-items producing a score which ranges from 11 to 44 with higher scores representing higher kinesiophobia. Scores greater than 37 are considered a high degree of kinesiophobia [49]. The reliability and validity of TSK-11 have been established [50].

Health-related quality of life was quantified using the European Quality of Life—Five Level (EQ-5D) scale that produces a single index value of range 0 to 1 where 1 is perfect health, and a VAS score ranging between 0 and 100, representing 'worst' to 'best' imaginable health state, respectively [51]. The EQ-5D, with each item having 5 possible responses, has improved inter-observer [ICC 2,1 0.57] and test-retest [ICC 2,1 0.69] reliability compared to the previous EQ-5D with three levels only [52]. The EQ-5D exhibits excellent psychometric characteristics across a wide variety of populations including musculoskeletal conditions [53].

Borg's scale (6–20) [54] was used to assess participants perceived effort performing submaximal contractions of their neck muscles.

2.5. Testing Procedures

Initially, all participants completed baseline self-reported outcomes, prior to physical data collection (Table 1). All participants, including healthy controls, provided their demographics and completed measures of neck disability (NDI), kinesiophobia (TSK), and quality of life (EQ-5D). Further questionnaires related to previous pain episodes

p e i ou and CNP
e p

e 1 S a c d a r s a

Data Collectio P nt	D	ab		t	o
aseline	e	ge			✓
		G d r		✓	✓
		g t		✓	✓
		W	✓		✓
	Pa ted m a u	N			
		S		✓	✓
		Q D		✓	✓
	thers	p	✓		
		A e i ep s des (VAS			
		k d			
		r n p y			
	Ob e i e measu	n m s (R M v i y, d o)		✓	✓
		opr c p i			
		Peak score of craniocervical flexion es	✓	✓	✓
		Muscle activity during submaximal CCF contractions	✓	✓	✓
		Max m m ck strengt i flex n and extension MVC flexion and extension [kg])	✓	✓	✓
		Perceived exertion during the submaximal task in flexion and extension (Borg's scale)	✓	✓	✓
Outcome measures	Questionnaires	Number of days with pain	✓		
		Neck Disability Index (NDI)	✓		

RNP: recurrent neck pain; CNP: chronic neck pain; ✓: collected data.

2.5.1. Cervical Kinematics

Physical testing was conducted by a physiotherapist in a quiet room. Each test was carried out with the participant seated in a chair with their arms supported and their feet on the ground. The assessor fixed an Inertial Measurement Unit (IMU; Noraxon USA Inc., Scottsdale, AZ, USA) on the middle of patient's forehead and another over the thoracic spine (T1); the sensors were calibrated to zero with the head in a natural position. Participants were then instructed to perform active neck movements as far as possible, at a self-paced natural speed, since most daily activities are performed at a natural speed [22,55]. This approach is consistent with what has been described in previous studies [21,56].

The directions of the head movements were performed in the same order among participants. Firstly, active neck flexion/extension was performed by instructing the participant to look forward, then fully flex and extend their neck continuously over 10 cycles (repetitions) without stopping. The choice of 10 repetitions for neck movements was selected in accordance with previous studies involving people with neck pain [57] and healthy volunteers [58]. Furthermore, this reasonably large number of repetitions was necessary to produce a representative sample of natural head motions, yet without inducing dizziness [57].

Similar procedures were applied to the active rotation task, where participants performed 10 cycles of continuous right to left rotations. Participants were instructed to perform all movements at a pace that is similar to what they perceive as a normal speed. A short rest of 1 min was given between each movement direction, with a longer period provided if requested, although this was not required.

2.5.2. Neck Proprioception

Once cervical kinematic examinations were completed, a rest of 3 min was provided, after which neck proprioception was assessed. Participants performed three repetitions of right and left neck rotation and in each trial, they were instructed to memorize a self-selected neutral position (starting position), close their eyes, and perform active head rotation after which they should return to the starting position as accurately as possible. All participants performed the proprioception test in the same order by alternating between right and left rotation with a rest period of one minute between each movement. The total testing time for the assessment of active neck movement and proprioception was approximately 15 min.

2.5.3. Craniocervical Flexion

Tests of craniocervical flexion were performed involving two Maximum Voluntary Contractions (MVCs) of craniocervical flexion followed by four submaximal contractions (20%, 40%, 60%, 80, and 100% of MVC). To assess the MVC, craniocervical flexion strength testing was performed with the participant lying supine with the hip and knees flexed to approximately 90 degrees [13]. The head was placed in neutral position and a dynamometer (NOD; OT Bioelettronica, Turin, Italy) was placed behind the upper cervical region with the instruction "to nod as if saying yes but as hard as you can, without lifting the head off the bed". Each maximum MVCs lasted 3 s, separated by 1 min rest in between repetitions [59].

In the same position described for the MVC, participants were instructed to perform craniocervical flexion at 20%, 40%, 60%, and 80% of their maximal force, attempting to hold the force for 10 s at each level. Visual feedback on force displayed on a tablet was used to guide the participant to reach and maintain the target force for the duration of the contraction. During this task, the amplitude of sternocleidomastoid (SCM) activity was measured with electromyography (EMG) (see details below).

2.5.4. Maximal Neck Extension/Flexion (Isometric Contractions)

Two MVCs of both neck flexion and extension were performed using a Multi-Cervical Unit (MCU) (BTE Technologies Inc, Hanover, MD, USA); each MVC lasted 3 s with one minute rest in between. Participants were comfortably seated on the chair of the MCU with their hips and knees flexed to 90 degrees, their head in neutral position and feet flat on the MCU stand. To measure neck flexion strength, the load cell of the MCU was placed over the forehead and the participant was instructed to "push as hard as you can as you try to bring your chin to your chest" [18]. Once two trials were completed, the load cell was then placed on the back of the head and the patient was instructed to "push as hard as you can into the load cell as if trying to bring the back of the head to your neck" [18].

In the same positions described for the MVC, the participants were instructed to perform a single submaximal contraction at 20% of their maximal force and hold this for 10 s for both neck flexion and extension. During these tasks, the amplitude of both SCM and splenius capitis (SC) activity was recorded with EMG.

2.6. Instrumentation

2.6.1. Inertial Measurement Unit

Neck kinematic and proprioception assessments were collected using a wearable IMU (Research PRO IMU, Noraxon USA Inc., Scottsdale, AZ, USA), with a sampling rate of 100 Hz. The dimensions of the sensor are 37.6 × 52 × 18.1 mm, and its mass is 34 g. The two sensors were fixed over the participants' forehead and thoracic spine (T1) [22], using double-sided tape. The signal was acquired using the software myoRESEARCH 3.12 (Noraxon USA Inc., Scottsdale, AZ, USA).

2.6.2. NOD Dynamometer and Multi-Cervical Unit (MCU)

Neck flexion and extension force was measured with the MCU (BTE Technologies Inc., Hanover, MD, USA). The reliability of measuring cervical strength with the MCU has been established (ICC ranging from 0.92 to 0.99) in individuals with neck pain [60]. Craniocervical flexion force was measured using a NOD device (OT Bioelettronica, Turin, Italy), a hand-held dynamometer.

2.6.3. Electromyography Analysis

Surface EMG (Ultium® EMG System, Noraxon USA Inc., Scottsdale, AZ, USA) was acquired from the SCM and SC bilaterally during the maximal and submaximal neck flexion and extension contractions whereas SCM only was measured during the submaximal craniocervical flexion contractions.

The skin was first shaved, if needed, rubbed with gel (Nuprep, Weaver and Company) and then washed with water using cotton wool. Noraxon dual EMG wet-gel electrodes (EMG electrodes, Noraxon USA Inc., Scottsdale, AZ, USA) were utilised which are disposable, wet-gel, self-adhesive Ag/AgCl snap electrodes. The electrode has an adhesive area of 40 mm × 22 mm, with dual circular electrodes of 10 mm diameter, and a fixed inter-electrode distance of 20 mm. Electrodes were placed "over the distal one-third of the muscle (sternal head)" [61] for the SCM muscle, and "at C2-C3 level between the uppermost parts of SCM and upper trapezius muscle" for the SC [62].

Raw data were collected via the Ultium EMG sensor (Noraxon USA Inc., Scottsdale, AZ, USA) using the Noraxon MyoMuscle software (myoRESEARCH, Noraxon USA Inc., Scottsdale, AZ, USA) which was then transferred to Matlab (Mathworks Matlab 2019b) for processing. EMG signals were low-pass filtered (pass band 20–400 Hz; order: 4) as used previously [63]. The EMG signals were sampled at 2000 Hz and converted with a 16-bit A/D converter.

2.7. Baseline Objective Measures (Candidate Predictors)

All data were analysed in Matlab (Mathworks Matlab 2019b). Signals related to neck movement were low-pass filtered (cut-off frequency of 10 Hz; order: 10) before computing the kinematic features. The start and end of the movement were defined as the time when the angular velocity exceeded a threshold of 5% of the peak velocity [22]. Although some studies used a threshold of 10% of the peak velocity to determine the start and stop of movement, using a threshold of 5% was deemed appropriate since we hypothesized that patients with RNP and CNP may present with lower peak velocity, therefore minimizing loss of data during the analysis. Moreover, the choice of 5% threshold was tested on our data during the pilot study of this project and considered appropriated for retaining representative data.

Maximum neck RoM (°) was defined as the maximum range achieved during each repetition of flexion, extension, and right and left rotation. The mean value of the ten repetitions for each direction was calculated and included in the analysis.

Mean velocity (Vmean [°/s]) was determined as the mean angular velocity achieved over the five repetitions for each movement direction. The average of the ten values was included in the analysis for each movement direction.

Peak velocity (Vpeak [°/s]) refers to the highest velocity value for each movement; the average of the ten repetitions were included in the analysis for each movement direction.

Number of velocity peaks (NVP [n]) refers to the number of times that the angular acceleration curve crossed zero. Details of this are reported elsewhere [64]. The average NVP that occurred across the ten repetitions were combined and included in the analysis for each movement direction.

Joint position error (JPE [°]) refers to the difference in degrees between the participants head position upon repositioning and the start location. The mean value of the three repetitions for each direction was calculated and included in the analysis.

Maximum craniocervical flexion strength (CCF MVC [Newton: N]) refers to the highest score achieved following the two maximal isometric contractions. Muscle activity during submaximal CCF contractions refers to the normalized EMG amplitude achieved during each of the four levels of submaximal isometric contractions (20%, 40%, 60%, and 80% of CCF MVC force). A 1 s sliding window was used to estimate the amplitude as a maximal root mean square (RMS) [65]. Two RMS values (for the right and left SCM) were obtained for each level of submaximal isometric contraction and these values were then normalized relative to the maximum EMG amplitude measured during the CCF MVC. The mean of both normalized values (right and left SCM) was included in the analysis [66].

Maximum neck strength in flexion and extension (MVC flexion and extension [kg]) refers to the peak force achieved following the two repetitions of each maximal neck isometric contractions.

Perceived exertion during the submaximal task in flexion and extension (Borg's flexion and extension) refers to the value of perceived exertion assessed on Borg's scale (6–20) [54] recorded immediately after completing the submaximal isometric contraction in flexion and extension at 25% MVC sustained for 30 s.

2.8. Outcome Measures for the Longitudinal Analysis (Prediction Model)

Two outcome measures were used to evaluate the predictive ability of physical and psychological measures (Table 1) in patients with RNP following a whiplash injury. All outcomes were treated as continuous variables without dichotomisation. This approach follows the recommendations of the PROGRESS series, that analysis of continuous variables be on a continuous scale [67]. This method increases the statistical power and reduces information loss.

To collect the outcome measures in this study, for each month of a 12-month follow-up, participants were instructed to record their neck disability, number of days with neck pain, and the average pain intensity during the previous month. These data were recorded each month using the electronic system Research Electronic Data Capture (REDCap) which enables researchers to monitor and manage the data collection process via a web interface [68]. The system provided an individualised link, involving the outcome measures, that was sent automatically each month for each participant.

2.8.1. Primary Outcome

The NDI score was selected as the primary outcome, which was assessed six months following baseline assessments. Using six months as a cut-off for identifying outcome was selected a priori [69,70]. NDI is widely used to evaluate perceived neck disability in people who have sustained a whiplash injury [71,72], and is a reliable and valid outcome [47].

2.8.2. Secondary Outcome

The secondary outcome was the number of days with pain. The mean number of days with pain over the course of 12 months considered. This outcome was defined as the number of days with neck pain during the previous month that lasted at least 24 h, with pain intensity of at least 20/100 on a VAS. This was measured using the questions 'Over the past month, how many days have you experienced neck pain?' and 'Over the past month, how would you rate your average neck pain intensity?'. The response for the first question is an absolute number, while a VAS score (0–100) was used to quantify pain intensity. The outcome and its definition have been used before by participants with low back pain [73], although pain intensity was assessed on a scale from 0–10. The selection of this outcome is of clinical importance as it captures pain that is relevant to the patients [74]. The mean number of days with pain per participant across the 12-month follow-up period was included in the analysis.

2.9. Sample Size

A sample size of 50 participants with RNP, 15 with CNP, and 15 healthy controls was initially planned. These numbers were not achieved, except for the control group, due to the COVID-19 pandemic which severely disrupted data collection for this project. Nevertheless, the current sample size is comparable to similar research that examined the same spine kinematic and neuromuscular characteristics in patients with neck [22] and/or low back pain [75].

2.10. Statistical Analyses

2.10.1. Cross-Sectional Analysis

Descriptive statistics were performed for participant demographics, and the data from self-reported questionnaires, cervical kinematic features, proprioception, and maximal and submaximal tasks. The normality of data distribution for self-reported and objective measures was assessed using the Shapiro–Wilk test. If data were not normally distributed for the measure of interest ($p \leq 0.05$), differences among groups were assessed using the Kruskal–Wallis test, after which a post hoc test (Dunn's test) was performed for making multiple pairwise comparisons.

If data were normally distributed ($p \geq 0.05$) for a measure, the following steps were conducted. Initially, homogeneity of variance was assessed using Levene's test for equality of variances. If a feature was homogenous (Levene's test value: $p \geq 0.05$), results from one-way analysis of variance (ANOVA) were used. When a feature was non-homogenous (Levene's test value: $p \leq 0.05$), results from a Welch ANOVA were used. Finally, a Tukey post hoc test was performed following one-way ANOVA, while Games–Howell post hoc test was used following Welch ANOVA.

2.10.2. Longitudinal Analysis

To identify the predictive value of baseline measurements on NDI at 6 months and on future episodes with neck pain over 12 months period, a two-step modelling approach was used [76]. Firstly, least absolute shrinkage and selection operator (LASSO) regression was used to reduce the number of candidate predictors entering into second stage analysis. A fivefold cross-validation was used in this study, considering the sample size. Further details about LASSO regression [69,77,78] and cross-validation [79] have been reported elsewhere. LASSO regression was used in the current study as it is feasible for estimating models with multiple predictors in a small sample size [80] and avoiding overfitting the data [81]. The analysis was performed on all baseline candidate predictors reported in Table 1. Candidate predictors with no predictive power or those that were highly correlated were penalized and reduced to zero. This penalisation (shrinkage) approach is used to effectively exclude candidate predictors from the final model by shrinking their coefficients to exactly zero [77]. Candidate predictors with zero coefficients were excluded from entering stage two. The second step was to perform multivariate linear regression analysis on candidate predictors with regression coefficients of more than zero that were identified from LASSO (first stage). R statistical software was used to conduct this analysis. The functions, packages, and codes that were used to analyse this data have been described elsewhere [82].

For this study, data from individuals with full cases for each model were considered. As a result, the observation number differs between models. This approach was used previously in [83]. For example, 17 participants with complete data were considered to develop the model with NDI, while 19 were considered for the model involving the outcome of number of days with pain.

Multiple imputations to deal with missing data in this study were not used. This is because all missing data were in the dependent variables (outcomes). Moreover, according to a previous study, multiple imputation is unnecessary for analysing longitudinal data as findings showed that multiple imputation was highly unstable when the multiple imputations were repeated 100 times [84].

The mean squared error (RMSE) [85] was used to quantify the prognosis error between predicted and observed values in each generated prognostic model. This is a measure to assess the internal validity of a model [86]. RMSE is interpreted on the same scale of an outcome. For example, NDI scores range from 0 to 50, and therefore RMSE can range from 0 to 50 too.

3. Results

3.1. Characteristics of Participants

Demographic characteristics and results for the self-reported questionnaires at baseline are reported in Table 2, with further figures available in the Supplementary Materials. Mean age (SD) was 31.1 ± 5.0 for the healthy participants, 31 ± 11.8 for RNP, and 33.6 ± 8.7 for those with CNP; the majority were females in all three groups. No significant differences were observed in participant demographics, except for height ($p = 0.02$). The mean score of average neck pain intensity for those with RNP during an episode (56.4 ± 14.5) and those with CNP (56.1 ± 19.5) was similar.

Table 2. Baseline characteristics of all three groups.

	Groups			*p*-Value
	Healthy Control (*n* = 15)	RNP (*n* = 22)	CNP (*n* = 8)	
	Mean ± SD	Mean ± SD	Mean ± SD	
Age (years)	31.1 ± 5.7	31.0 ± 11.8	33.6 ± 8.7	0.24 [1]
Gender (male:female (%))	6:9 (60%)	8:14 (64%)	1:7 (88%)	0.38 [2]
Height (m)	1.7 ± 0.1	1.7 ± 0.1	1.6 ± 0.1	0.02 [3]
Weight (kg)	69.1 ± 14.8	74.7 ± 18.0	59.5 ± 9.8	0.07 [1]
NDI (0–50)	0.7 ± 1.1	5.5 ± 3.2 *	17.5 ± 7.6 *,†	<0.001 [1]
TSK (17–68)	29.1 ± 4.3	35.2 ± 5.5 *	40.5 ± 7.5 *	<0.001 [3]
EQ-5D (0–1)	0.98 ± 0.04	0.92 ± 0.09 *	0.68 ± 0.21 *,†	<0.001 [1]
EQ VAS (0–100)	85.5 ± 10.2	78.5 ± 15.4	64.1 ± 14.4 *,†	0.005 [1]
Number of pain episodes, 12 m	-	5.9 ± 4.4	-	
Average of pain episodes, VAS (0–100)	-	56.4 ± 14.5	-	
Current neck pain, VAS (0–100)	-	-	56.1 ± 19.5	
Neck pain duration, m	-	-	39.1 ± 41.4	

SD: standard deviation; NDI: Neck Disability Index; TSK: Tampa Scale of Kinesiophobia; EQ-5D: European Quality of Life—5 Dimensions; EQ-VAS; self-rated health on a vertical visual analogue scale; VAS: Visual Analogue Scale. [1] Kruskal–Wallis Test. [2] Chi-square Test. [3] One-way ANOVA (Bonferroni post hoc shows significant group difference in height between healthy and CNP [$p < 0.02$], and RNP and CNP [$p < 0.03$]). * Post hoc significant difference from control group at $p < 0.05$. † Post hoc significant difference from RNP group at $p < 0.05$.

Descriptive statistics of the self-reported questionnaire measured at baseline for the three groups are provided in Table 2. Neck disability measured by the NDI (χ^2 (2) = 32.34, $p < 0.0001$) and quality of life by EQ-5D (χ^2 (2) = 23.03, $p < 0.0001$) were significantly different across all three groups. Patients with CNP presented with the highest disability (17.5 ± 7.6), followed by RNP (5.5 ± 3.2), and healthy controls who had almost no disability as expected (0.7 ± 1.1). The opposite was observed for quality of life where participants with RNP (0.92 ± 0.09), and CNP (0.68 ± 0.21) had significantly lower scores compared to healthy controls (0.98 ± 0.04), indicating lower quality of life. The Tukey post hoc comparison test revealed significant differences in TSK between those with RNP and healthy controls ($p < 0.001$), and between CNP and healthy controls ($p < 0.0001$), but not between RNP and CNP (Table 2). Significant differences were observed for EQ-VAS between RNP and CNP ($p < 0.05$), and between healthy controls and CNP ($p < 0.001$).

3.2. Cervical Kinematics and Proprioception

The descriptive statistics and the results of the one-way ANOVA for cervical kinematics and proprioception are reported in Table 3. People with RNP showed no significant differences when compared to healthy or CNP groups in RoM, but significant differences were observed between CNP and controls in combined RoM in flexion and extension ($p < 0.05$), and combined right and left rotation ($p < 0.05$). JPE following right ($\chi^2(2) = 0.08$, $p = 0.96$) and left ($\chi^2(2) = 0.58$, $p = 0.75$) rotations were not significantly different among groups. Mean velocity was significantly lower in those with RNP and CNP than healthy controls during neck flexion ($\chi^2(2) = 12.98$, $p = 0.0015$) right rotation ($F(2,39) = 5.24$, $p = 0.01$), and left rotation ($F(2,39) = 5.53$, $p = 0.008$), but not during neck extension ($\chi^2(2) = 4.81$, $p = 0.09$). Neither group with neck pain showed significant differences in mean velocity during any movement direction.

Table 3. Summary statistics for the kinematic and proprioception features of all three groups with differences assessed using One-way ANOVA.

	Groups			
	Healthy Control (*n* = 15) Mean ± SD	**RNP (*n* = 22) Mean ± SD**	**CNP (*n* = 8) Mean ± SD**	***p*-Value**
Flexion				
Vmean (°/s)	72.8 ± 12.3	55.0 ± 18.5 *	42.9 ± 14.3 *	0.002 [1]
Vpeak (°/s)	149.5 ± 33.9	114.0 ± 41.3 *	90.8 ± 28.8 *	0.004
NVP (*n*)	9.4 ± 4.0	17.1 ± 9.4 *	17.5 ± 8.2	0.005 [2]
Extension				
Vmean (°/s)	66.5 ± 15.7	55.4 ± 21.2	46.7 ± 16.5	0.09 [1]
Vpeak (°/s)	133.8 ± 31.5	111.0 ± 45.1	97.2 ± 34.4	0.12
NVP (*n*)	8.3 ± 4.1	17.8 ± 14.0	16.5 ± 9.0	0.066 [1]
Right Rotation				
Vmean (°/s)	132.5 ± 29.3	101.5 ± 41.7 *	82.5 ± 22.0 *	0.001 [2]
Vpeak (°/s)	244.7 ± 52.5	190.5 ± 76.7	157.1 ± 37.9 *	0.001 [2]
NVP (*n*)	5.1 ± 3.3	8.6 ± 9.1	10.2 ± 6.5	0.017 [1]
JPE	3.8 ± 2.1	4.4 ± 2.5	5.5 ± 5.9 *	0.76 [1]
Left Rotation				
Vmean (°/s)	131.2 ± 30.7	100.1 ± 41.0 *	79.5 ± 22.6 *	0.001 [2]
Vpeak (°/s)	244.5 ± 57.2	188.8 ± 71.7 *	148.7 ± 34.7 *	<0.001 [2]
NVP (*n*)	3.7 ± 2.8	9.0 ± 8.8	11.6 ± 10.5	0.014 [1]
JPE	4.2 ± 2.8	4.7 ± 2.8 *	5.2 ± 5.2 *	0.711 [1]
Combined RoM				
Flexion/Extension	52.6 ± 8.1	49.5 ± 7.9	42.9 ± 10.2 *	0.041
Right/Left Rotations	71.5 ± 6.2	67.1 ± 9.4	62.1 ± 9.1 *	0.042

SD: standard deviation; SD error: Standard error (of the mean); CI: confidence intervals; RoM: Range of motion; Vmean: mean velocity; Vpeak: peak velocity; Vpeaks: mean of peaks velocity; NVP: number of velocity peaks; JPE: joint position error. [1] Differences were assessed using Kruskal–Wallis ANOVA. [2] Differences were assessed using Welch's ANOVA. * Post hoc significant difference from control group at $p < 0.05$.

The NVP were higher (less smooth movement) in all directions in those with RNP and CNP compared to healthy controls. However, significant differences for the RNP group were only observed during flexion and left rotation ($p < 0.05$), and during both rotations for those with CNP ($p < 0.05$). Both groups with neck pain showed similar NVP with no significant difference between groups.

3.3. EMG Amplitude Assessed during Submaximal CCF Contractions

Maximum CCF strength did not differ across groups ($p = 0.57$). The activity of SCM during the submaximal CCF contractions at 60% MVC was significantly different between people with CNP and RNP ($p < 0.01$) and between CNP and healthy controls ($p < 0.01$). No other significant differences were found. Data are summarised in Table 4.

Table 4. Normalized EMG amplitude (%) recorded from sternocleidomastoid muscles during each of the five submaximal craniocervical flexion contractions in addition to the maximum craniocervical contraction.

	Groups			
	Healthy Control (*n* = 15) Mean ± SD	**RNP (*n* = 22) Mean ± SD**	**CNP (*n* = 8) Mean ± SD**	***p*-Value**
Normalized EMG amplitude (%)				
20%	18.8 ± 12.0	33.6 ± 22.6	52.0 ± 53.1	0.11 [1]
40%	35.2 ± 23.9	64.3 ± 88.5	70.8 ± 36.5	0.07 [1]
60%	50.9 ± 15.9	58.7 ± 29.0	111.8 ± 80.1 *,†	0.003
80%	66.9 ± 21.7	79.0 ± 33.6	108.6 ± 88.4	0.34 [1]
Maximum craniocervical contraction				
CCF MVC (N)	52.1 ± 22.3	44.0 ± 23.4	47.1 ± 22.8	0.57

SD: standard deviation; SD error: standard error (of the mean); CI: confidence intervals, CCF MVC: maximum craniocervical flexion strength; N: Newton (unit of force). Numbers are presented as normalized EMG (%). [1] Kruskal–Wallis ANOVA. * Post hoc significant difference from control group at $p < 0.05$. † Post hoc significant difference from RNP group at $p < 0.05$.

3.4. Maximal Neck Strength and Perceived Fatigue

A significant difference was observed between people with RNP and controls for neck extension strength ($p < 0.05$), but with no significant difference between RNP and CNP groups. No difference in neck flexion strength was observed between groups. People with RNP and CNP displayed similar greater perceived exertion in flexion and extension. Perceived exertion assessed during the submaximal isometric neck flexion was significantly different between those with RNP and controls ($p < 0.01$). Results are summarised in Table 5.

Table 5. Results of neck strength during the isometric contraction and perceived fatigue during submaximal contraction in MCU.

	Groups			
	Healthy Control (*n* = 15) Mean ± SD	**RNP (*n* = 22) Mean ± SD**	**CNP (*n* = 8) Mean ± SD**	***p*-Value**
Maximal strength (MVC)				
Flexion MVC (kg)	20.2 ± 9.7	14.6 ± 6.4	15.3 ± 3.1	0.17 [1]
Extension MVC (kg)	29.6 ± 18.5	15.3 ± 4.4 *	21.6 ± 9.1	0.006 [1]
Rate of perceived exertion (BORG scale: 6–20)				
Flexion Borg (6–20)	12.0 ± 3.1	15.0 ± 3.0 *	14.7 ± 1.7	0.01
Extension Borg (6–20)	8.9 ± 2.5	9.9 ± 2.5	10.4 ± 2.6	0.38 [1]

SD: standard deviation; SD error: standard error (of the mean); CI: confidence intervals; MVC: maximal voluntary contraction. [1] Kruskal–Wallis ANOVA. * Post hoc significant difference from control group at $p < 0.05$.

3.5. Participant Follow-Up through the Longitudinal Analysis

The total numbers of participants who completed the follow-up questionnaires at each month are reported in Figure 1. From 22 participants who participated at baseline, 17 (77%) participants completed the NDI at six months, whereas 19 (86%) completed the outcomes related to number of days with pain.

Two participants did not complete any of the 12-month follow-up questionnaires despite the maximum of three reminders. The highest completion rate of follow-up was at the first month (n = 20; 91%), whereas the lowest was at 12 months (n = 16; 73%). One participant withdrew from the study at three months without providing any reason. No significant differences in baseline characteristics were present between the participants who dropped out and those included in the current study.

3.5.1. Characteristics of Participants

Self-reported outcomes indicated that, on average over the 12 months, people complained of neck pain for an average of five days per month. The mean of monthly number of days with pain for all participants is illustrated in Figure S8. Mean neck disability assessed by the NDI was (mean ± SD) of 8.6 ± 5.0 at six months.

3.5.2. Step 1: Predictor Variable Selection (i.e., Shrinking the Number of Predictors)

The baseline covariates for both outcomes (NDI and future episodes of neck pain) that had nonzero coefficients are reported in Table 6. Using LASSO, the number of predictors for the outcome NDI at six months was reduced from fifteen to two predictors including MVC in flexion and previous number of days with pain. For predicting the outcome future episodes of neck pain at one year, the number of predictors was reduced from fifteen to one which was previous number of pain episodes. These variables for the two outcomes were included in the multivariate regression analysis in the next step. Graphs of the reduction in number of predictors achieved by applying LASSO are available in the Supplementary Materials (Figures S9 and S10).

Table 6. Selected predictor variables for response variable of number of days with pain.

	NDI at 6 Months	Number of Days with Pain
(Intercept)	8.65	4.68
NDI	0	0
TSK	0	0
EQ-VAS	0	0
EQ-5D	0	0
Previous number of pain episodes	0.68	0.57
Average of pain episodes	0	0
ROM in flexions and extension	0	0
ROM in rotations	0	0
NVP in flexions and extension	0	0
JPE	0	0
20% and 40 of CCF MVC force	0	0
60%, and 80% of CCF MVC force	0	0
CCF MVC	0	0
MVC during cervical flexion	−0.34	0
MVC during cervical extension	0	0

NDI: Neck Disability Index; TSK: Tampa Scale of Kinesiophobia; EQ-5D: European Quality of Life—5 Dimensions; EQ-VAS; self-rated health on a vertical visual analogue scale; RoM: range of motion; NVP: number of velocity peaks; JPE: joint position error; CCF MVC: maximum craniocervical flexion strength; MVC: maximal voluntary contraction.

3.5.3. Step 2: Prediction Model Development

Prediction of Neck Pain and Disability at Six Months

A multiple regression was run to predict NDI at six months from MVC during flexion and previous number of neck pain episodes. These variables significantly predicted the NDI at six months, $F(2,14) = 6.97$, $p = 0.008$, $R^2 = 0.50$. Both variables added significantly to the prediction model and are reported in Table 7. A one-kg reduction in MVC in flexion significantly increased NDI by 0.32 units ($t = -2.21$, $p = 0.04$, 95% CI: [−0.64]–[−0.01]). A single episode of neck pain within the last 12 months significantly predicted an increase in NDI by 0.54 units ($t = 2.56$, $p = 0.02$, 95% CI: 0.09–0.99). This model explained 43% of the variability in NDI at six months. This model resulted in a RMSE of 3.47 meaning that the NDI values that were predicted by this model differed from the observed values of NDI by 3.47 (Figure 2A).

Table 7. Results of multivariate regression analysis showing associations between baseline predictors and NDI at six months.

	β	SE	*t* Value	*p* Value	Low 95%CI	Upper 95% CI	Adjusted R^2
(Intercept)	10.23	2.99	3.42	0.004	3.82	16.63	0.43
MVC flexion	−0.32	0.15	−2.21	0.04	−0.64	−0.01	
Previous number of pain episodes	0.54	0.21	2.56	0.02	0.09	0.99	

β: unstandardized coefficient; SE: standard error; CI: confidence interval; Adjusted R^2: represents the variance in NDI (the outcome) as explained by the variables; MVC: maximum voluntary contraction. $n = 19$; 86% with complete cases

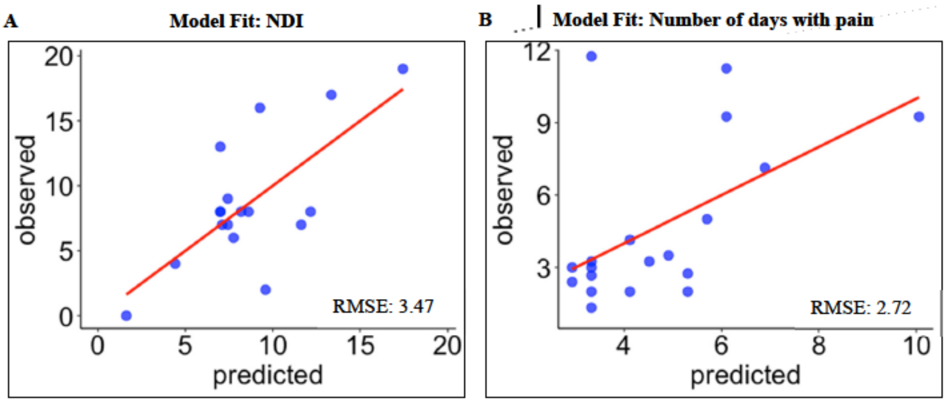

Figure 2. Scatterplots of two models fit comparing the predicted and observed values for each outcome: NDI: Neck Disability Index at six months (**A**) and number of days with pain over the 12-month follow-up period (**B**). The diagonal line in red indicates perfect prediction. RMSE: root mean square error, which represents the error between predicted and observed values in each generated prognostic model. Lower values of RMSE indicate better prediction.

Prediction of Future Episodes of Neck Pain over the 12-Month Follow-Up Period

A multiple regression was run to predict future episodes of neck pain within the next year, from previous number of pain episodes. This variable resulted in a statistically significant model predicting future episodes of neck pain, $F(1,17) = 6.93$, $p = 0.017$, $R^2 = 0.29$. A single episode of neck pain within the last 12 months significantly predicted a future episode by 0.40 unit ($t = 2.63$, $p = 0.02$, 95% CI: 0.08–0.71) (Table 8). This model explained 25% of the variability in future episodes of neck pain. The RMSE for this model was 2.72, representing the differences in number of days between the predicted and observed values (Figure 2B).

Table 8. Results of multivariate regression analysis showing associations between baseline predictors and number of days with pain (average of 12 months).

	β	SE	*t* Value	*p* Value	Low 95%CI	Upper 95% CI	Adjusted R^2
(Intercept)	2.14	1.17	1.83	0.08	−0.33	4.61	0.25
Previous number of pain episodes	0.40	0.15	2.63	0.02	0.08	0.71	

β: unstandardized coefficient; SE: standard error; CI: confidence interval; Adjusted R^2: represents the variance in number of days with pain (the outcome) as explained by the variable. $n = 17$; 77% with complete cases.

4. Discussion

This is the first study to conduct a comprehensive investigation of neuromuscular features including cervical kinematics, sensorimotor performance (proprioception), superficial neck muscle activity, neck strength, and subjective fatigue among individuals with CNP, RNP (following a whiplash injury), and healthy controls. The findings provide evidence that people with a history of neck pain, even when in remission from pain, present with similar psychological and neuromuscular function consisting of altered neck movement, increased activity of superficial neck muscles, lower neck muscle strength, and greater perceived fatigue during sustained contractions. Importantly, when examining the predictive capacity of these features, lower neck flexion strength together with a higher number of previous pain episodes within the last 12 months were predictors of higher neck disability at six months. This provides preliminary evidence that some aspects of neuromuscular function (namely lower neck strength) are relevant for predicting future neck pain and disability.

The current study showed that people with either CNP or RNP following a whiplash injury presented with higher disability, higher kinesiophobia, and lower quality of life compared to healthy controls. The presence of psychological features and poorer quality of life have been commonly reported previously for patients with chronic WAD [87]; however, this is the first study to demonstrate that people with frequent episodes of neck pain could present with disability, poorer quality of life and some degree of kinesiophobia despite being pain free.

4.1. Cervical RoM

A general trend of reduced RoM was observed for both the CNP and RNP groups although significant differences were only observed between CNP and controls. Reduced RoM either in all or some directions has been reported previously in patients with CNP [19], despite methodological differences between studies. Whilst not significant, the average cervical RoM was lower in people with RNP compared to the controls. This might be due to the small sample size in the current study, which could result in this study being underpowered for RoM. The extent of restricted cervical RoM in people with RNP has not been studied before [32], but restricted RoM in the thoracic and lumber spine was reported in people with recurrent low back pain [88–90]. However, unlike the current study, the studies on recurrent low back pain included participants that reported some degree of pain during the assessment [88,90]. Future research should further investigate the presence of changes in spine kinematics in people with RNP [32] in a larger sample size.

4.2. Velocity and Smoothness of Neck Movement

Individuals with CNP in the current study moved their neck slowly and with irregular movements when performing cervical rotations. These findings are similar to previous work showing that people with CNP, either from traumatic or non-traumatic causes, display more irregular and slower neck movement [19–22]. Such a pattern of movement could be interpreted as cautious movements to avoid neck pain [91]. These changes in how neck movements are performed are in line with current theories regarding how pain affects movement and motor control [91]. However, the current study uniquely showed that slower neck movement in flexion and rotation with irregular neck movements in flexion and left rotation can also be present even when pain is not present, i.e., during a period of remission in people with RNP. The driving mechanism for the altered movement performance (slow and irregular movement) during pain remission is not fully understood and further studies exploring these neuromuscular adaptations and their association to clinical features should be investigated.

4.3. Cervical Proprioception

In this study, neck proprioception was not significantly different between groups. This finding was also observed in previous studies of patients with persistent WAD, who have similar pain intensity to the cohort tested in the current study [92–94]. A recent meta-analysis, found that patients with chronic WAD have significant larger JPE following cervical rotation when compared to healthy controls, but there is a discrepancy between studies [16]. Such discrepancies could be attributed to various factors. For example, several studies have used different methods to assess JPE including a variety of measurement devices and sensor placements [95] that potentially influenced the findings. Moreover, people with chronic WAD presenting with dizziness or greater pain intensity tend to show greater deficits in sensorimotor control [96], and this was not accounted for in the current study. Finally, sensorimotor disturbances are highly variable between people with WAD in both the nature of impairments and their frequency of presentation [96] and thus our sample size may have not been sufficient to capture a difference.

4.4. EMG Amplitude Assessed during CCF Submaximal Contractions

The current study showed generally higher activity of the SCM in people with CNP compared to healthy controls, although significant differences were only seen at 60% MVC. Once again, the small sample size could be the reason for why this was significant at 60% only and not at other levels. Previous studies showed that people with CNP often display higher activation of the superficial neck flexors [13,15,97,98], which is negatively associated with the extent of activation of the deep neck flexors [66]. The effect of pain on coordination between the deep and superficial neck flexors is well documented [99–101], and such a phenomenon was also seen early in patients with acute neck pain following a whiplash trauma [17]. Notably, greater activation of the superficial neck muscles was generally seen in this study (albeit not significant) even during remission of pain in people with RNP following a whiplash injury. It could be hypothesised that there might be ongoing motor control deficits for these individuals which have not been specifically targeted during a period of rehabilitation. For example, studies have shown that neuromuscular dysfunction can persist despite the resolution of, or reduction in, pain following active interventions not specifically designed to alter neuromuscular control [102,103].

4.5. Maximal Neck Strength and Perceived Fatigue

Both groups with a history of neck pain displayed lower isometric neck flexion and extension strength, although significant differences were only observed in extension between people with RNP and controls. People with neck pain frequently present with lower neck strength [18,104–106], though the degree of impairment varies greatly between patients [107] and can be associated with features such as the degree of kinesiophobia [59] and current pain intensity [108]. Previous work has shown that, compared to healthy controls, individuals with persistent WAD have significantly lower isometric MVC force in extension, retraction, and lateral flexion [18]. However, the current study was not able to confirm these findings. These differences could be explained due to the natural variability in neck strength among participants [91]. A large range of neck strength values has beenshown previously in people with CNP, most likely reflecting the large heterogeneity observed among people with neck pain [18,109–111]. Another reason could relate to the level of disability, since strength deficits are typically larger in those with higher disability [18].

Besides lower neck strength, higher perceived fatigue during neck flexion (significantly different) was found in the group with RNP during the submaximal contraction at 25% MVC. Previous studies found evidence of greater neck extensor endurance than neck flexor endurance in people with idiopathic neck pain [112–114], which could explain why significant differences were observed in flexion only. Indeed, the CNP and RNP groups had a mean score of approximately 15 on Borg's scale in flexion compared to a mean of 10 for extension.

4.6. Predicting Neck Disability and Number of Days with Pain

In our sample, higher number of pain episodes within the last 12 months was a common predictor of higher neck disability and a higher number of days with pain. This finding is consistent with a previous prognostic study of people with RNP who were followed for one year [115]. The study found that a previous episode of neck pain predicted future recurrence of pain, which was defined as a new episode of neck pain [11]. Another study in people with low back pain confirmed the negative effect of a longer duration of a current episode on disability up to five years [116]. Nonetheless, no study has investigated this in people with RNP following a whiplash trauma, which warrants further investigation.

Besides the higher number of pain episodes, baseline lower isometric neck strength in flexion was identified as a predictive factor of higher disability at six months. Although not directly comparable to the current study, previous studies found similar findings in that muscle strength was a significant factor predicting future injury in the lower limb [117–120]. Lower neck strength in flexion was observed at baseline in patients with RNP, who presented on average with a reduction (−5.6 kg) in neck strength in flexion compared to healthy controls. These findings could emphasize the potential long-term effect of impaired neck strength and frequent episodes of neck pain on the development of neck disability. Further studies are needed to confirm this finding and investigate the interaction between neck muscle strength and future episodes of neck pain.

4.7. Model Performance

In this study, our models performed similarly to earlier machine learning prediction models. The first model in this study provided an estimate of the expected NDI values at six months with an average RMSE of 3.47 points, on a 0–50 scale. This score represents the average magnitude (error) of the difference between the observed NDI at six months and scores predicted by the model. In another words, it measures how close the observed data points are to the predicted model values where lower RMSE values reflect a better fit.

The RMSE score to predict NDI is similar to a model generated in people with cervical radiculopathy [82], with an RMSE of about 8.2% (NDI 0–100% scale). However, this comparison should be interpreted with caution due to the different populations. The other developed model in the current study showed that the average difference between predicted and observed values, indicated by RMSE, was 2.72 days with pain.

4.8. Clinical Implications

The current study provided evidence that people with RNP presented with changes in some neuromuscular and psychological features even during complete remission of pain. Furthermore, some of these changes were comparable to people with CNP. These findings could have significant implications for rehabilitation and prevention. For example, some of the features could be targeted in a rehabilitation program with the aim to promote restoration of altered function identified in this study and preventing recurrent episodes of neck pain. Commonly treatment is aimed at reducing pain, yet this work emphasises that restoration of neuromuscular function is equally relevant.

The longitudinal investigation in the current study showed that a higher number of previous pain episodes together with lower neck flexion strength predicted higher neck disability six months later. Neck strength is a modifiable feature. Thus, strengthening of the neck flexors in people with RNP may lower future neck disability although this needs to be tested in a longitudinal study. On the other hand, although the number of previous pain episodes is not a modifiable variable, this should be considered.

4.9. Strength and Limitations

This study has several strengths. This is the first study to examine physical features in a group of participants with RNP following a whiplash injury who were asymptomatic at inception. Moreover, a comprehensive battery of measures including demographic, psychological, and physical features were assessed at baseline. All these baseline features were then included as predictors of outcomes in people with RNP who were followed up over 12 months. A follow-up rate of more than 80% is desired in prognostic research [121]. This cut-off was fulfilled in one of the developing models including 86% follow-up rate across 12 months study period. For prognostic analysis, best practice recommendations were followed for the development and validation of the models [122,123].

There are some limitations to consider. One of the main limitations of this study is the sample size which could bias the results of this study. A sample size of 50 participants for RNP, 15 for CNP, and 15 for controls was planned in advance, but this was fulfilled only in the latter group. This was because of the COVID-19 pandemic which interrupted data collection. However, the current study was able to find some significant differences across groups and/or show a trend at baseline. Another potential limitation is that the number of female participants was higher than males in the group with CNP. However, no significant differences were observed in gender across groups as reported in Table 2. For prognostic analysis, a low sample size in the RNP group prevents us from separating the data into training and validation sets, the latter could be used in independent validation [123]. Furthermore, this smaller sample size compared to the high number of predictors could lead to overfitting of the developed models. However, this study incorporated LASSO, a powerful method that performs regularization and feature selection and can deal with a high number of predictors [124]. This is a unique study and it is difficult to determine the extent to which the results are generalizable, especially given that a convenience sample was adopted. Additionally, this study may not be generalizable to people with greater neck pain and disability as this was associated with general variability of neuromuscular adaptations [15,125,126]. This study included people with RNP and CNP who experienced minimal and mild to moderate pain and disability [46], respectively. Similarly, the higher level of kinesiophobia in people with CNP in the current study may not be generalizable to other cohorts with CNP who present lower levels of kinesiophobia. Restriction in the range and performance of neck movements could be influenced by kinesiophobia [127,128]. As a further consideration, it should be noted that kinesiophobia was the only measure of psychological function that was assessed in the current study and other features such as anxiety and depression may be relevant.

5. Conclusions

Participants with RNP during a period of remission presented with altered neuromuscular function and poorer psychological function, and several of these features were comparable to the presentation of people with CNP. These features included higher disability, higher kinesiophobia, and lower quality of life. People with RNP also performed slower and more irregular neck movements in most directions and displayed lower neck strength in extension and higher perceived fatigue in flexion. Some of these baseline variables were able to predict ongoing neck disability and days with pain in those with RNP when followed over 12 months. These included a higher number of previous pain episodes and lower neck flexion strength.

Supplementary Materials: The following supporting information can be downloaded at: https://www.mdpi.com/article/10.3390/jcm11072042/s1, Figure S1: Boxplots of NDI, TSK, EQ-5D, and EQ VAS of all three groups. Results of Post hoc tests between groups are presented; Figure S2: Boxplots of cervical movement of all three groups. Results of Post hoc tests between groups are presented; Figure S3: Boxplots of neck proprioception of all three groups. Results of Post hoc tests between groups are presented; Figure S4: Boxplots of mean velocity of all three groups. Results of Post hoc tests between groups are presented; Figure S5: Boxplots of smoothness of movement of all three groups. Results of Post hoc tests between groups are presented; Figure S6: Boxplots of normalized EMG recorded from SCM during submaximal craniocervical flexion task. Results of Post hoc tests between groups are presented; Figure S7: Maximal neck strength in flexion (A) and extension (B). Borg's scale was used to measure perceived fatigue during submaximal contraction at 20% MVC; Figure S8: line plot showing mean number of days with pain (outcome) over 12 months follow-up period; Figure S9: Results of the Least absolute shrinkage and selection operator involving all predictors with Neck Disability Index as an outcome at 6 months; Figure S10: Results of the Least absolute shrinkage and selection operator involving all predictors with days with pain over the 12-month follow-up period as an outcome. Table S1: STROBE Statement—Checklist of items that should be included in reports of cross-sectional studies.

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Supplementary Materials

Boxplots for self-reported questionnaire

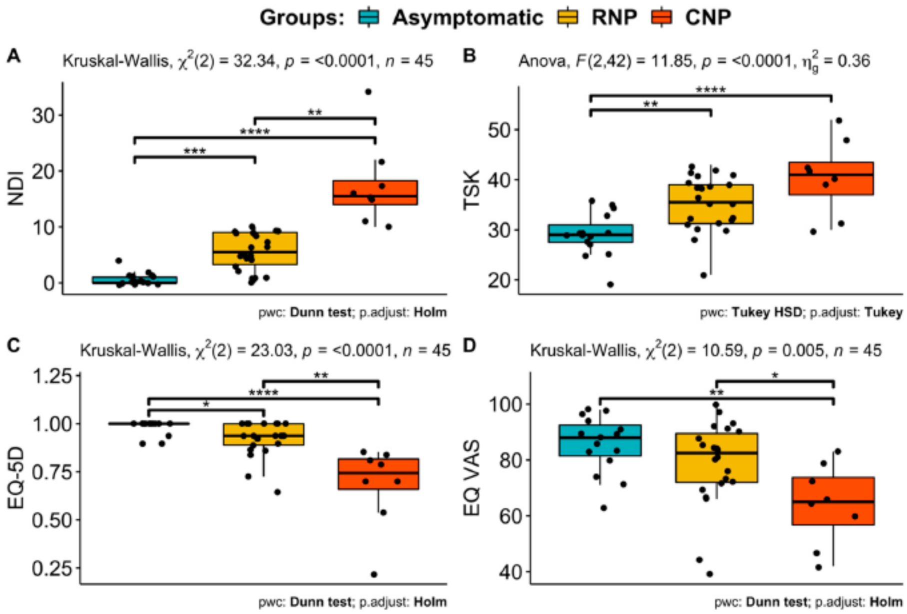

Figure S1: Boxplots of NDI, TSK, EQ-5D, and EQ VAS of all three groups. Results of Post hoc tests between groups are presented. *p<0.05, **p<0.01, *** p<0.001, **** p<0.0001
RNP: Recurrent Neck Pain; CNP: Chronic Neck Pain; NDI: Neck Disability Index; TSK: Tampa Scale of Kinesiophobia; EQ-5D: European Quality of life – 5 Dimensions; EQ-VAS; self-rated health on a vertical visual analogue scale; ; PWC: The post-hoc test used for the multiple pairwise comparisons; P.adjust: Method for calculating the adjusted p value.

Boxplots for cervical kinematics and proprioception

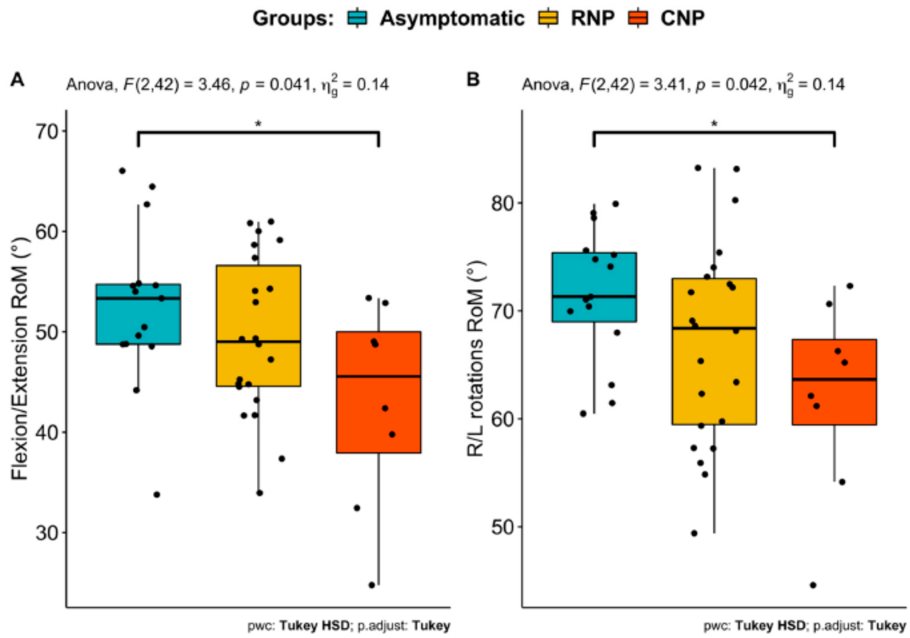

Figure S2: Boxplots of cervical movement of all three groups. Results of Post hoc tests between groups are presented; *p<0.05.
RNP: Recurrent Neck Pain; CNP: Chronic Neck Pain; RoM: Range of Motion; °: Degree; R/L: Right/Left; PWC: The post-hoc test used for the multiple pairwise comparisons; P.adjust: Method for calculating the adjusted p value.

Boxplots for joint position error

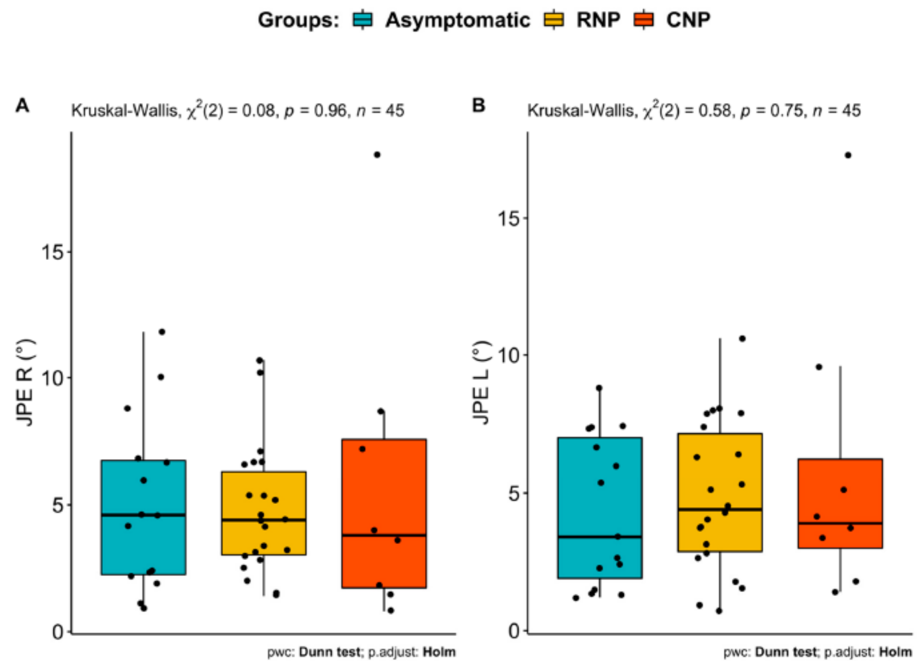

Figure S3: Boxplots of neck proprioception of all three groups. Results of Post hoc tests between groups are presented.
RNP: Recurrent Neck Pain; CNP: Chronic Neck Pain; JPE: Joint Position Error; °: Degree; PWC: The post-hoc test used for the multiple pairwise comparisons; P.adjust: Method for calculating the adjusted p value.

Boxplots for mean velocity in all directions

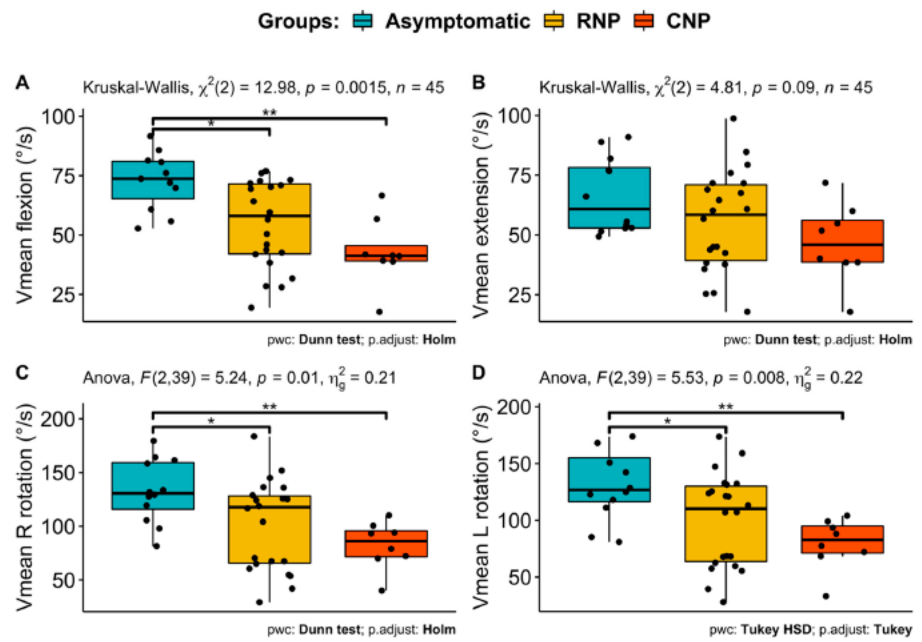

Figure S4: Boxplots of mean velocity of all three groups. Results of Post hoc tests between groups are presented; *p<0.05; **p<0.01.
RNP: Recurrent Neck Pain; CNP: Chronic Neck Pain; Vmean: Mean Velocity; °: Degree; S: Seconds; R: Right; L: Left; PWC: The post-hoc test used for the multiple pairwise comparisons; P.adjust: Method for calculating the adjusted p value.

Boxplots for number of velocity peaks in all directions

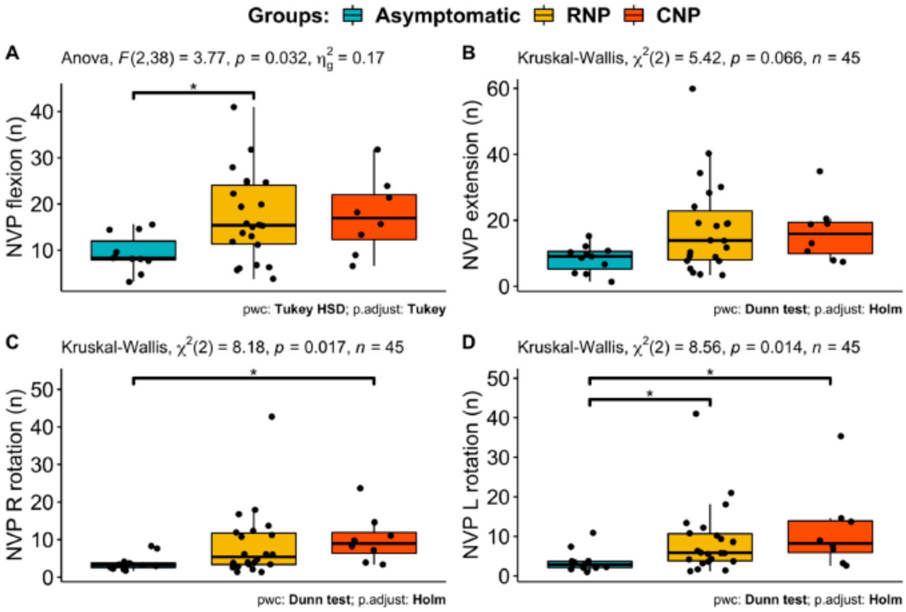

Figure S5: Boxplots of smoothness of movement of all three groups. Results of Post hoc tests between groups are presented. *p<0.05.
RNP: Recurrent Neck Pain; CNP: Chronic Neck Pain; NVP: Number of Velocity Peaks; n: Number; R: Right; L: Left; PWC: The post-hoc test used for the multiple pairwise comparisons; P.adjust: Method for calculating the adjusted p value.

Boxplots for EMG amplitude assessed during submaximal CCF contractions

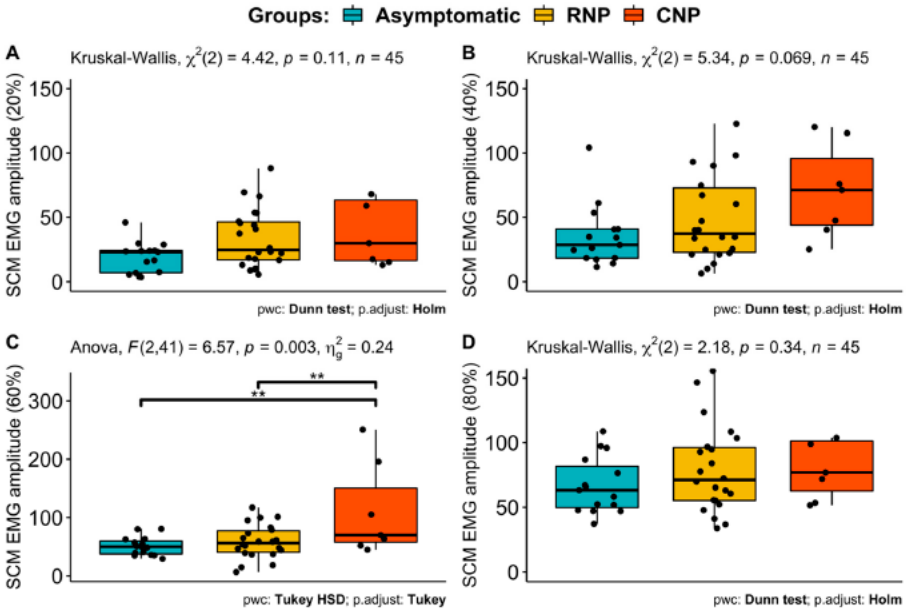

Figure S6: Boxplots of normalized EMG recorded from SCM during submaximal craniocervical flexion task. Results of Post hoc tests between groups are presented. **p<0.01.
RNP: Recurrent Neck Pain; CNP: Chronic Neck Pain; SCM: Sternocleidomastoid Muscles; EMG: Electromyography; PWC: The post-hoc test used for the multiple pairwise comparisons; P.adjust: Method for calculating the adjusted p value.

Boxplots for maximal neck strength and perceived fatigue

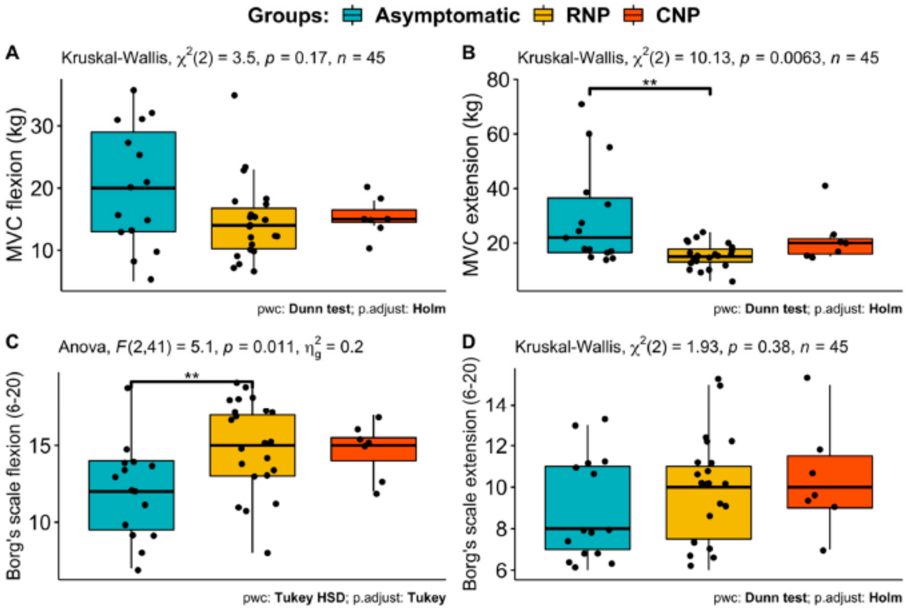

Figure S7: Maximal neck strength in flexion (A) and extension (B). Borg's scale was used to measure perceived fatigue during submaximal contraction at 20% MVC. **p<0.01.

RNP: Recurrent Neck Pain; CNP: Chronic Neck Pain; MVC: Maximum Voluntary Contraction: kg: Kilogram; PWC: The post-hoc test used for the multiple pairwise comparisons; P.adjust: Method for calculating the adjusted p value.

Mean values of number of days with pain over 12 months follow-up period

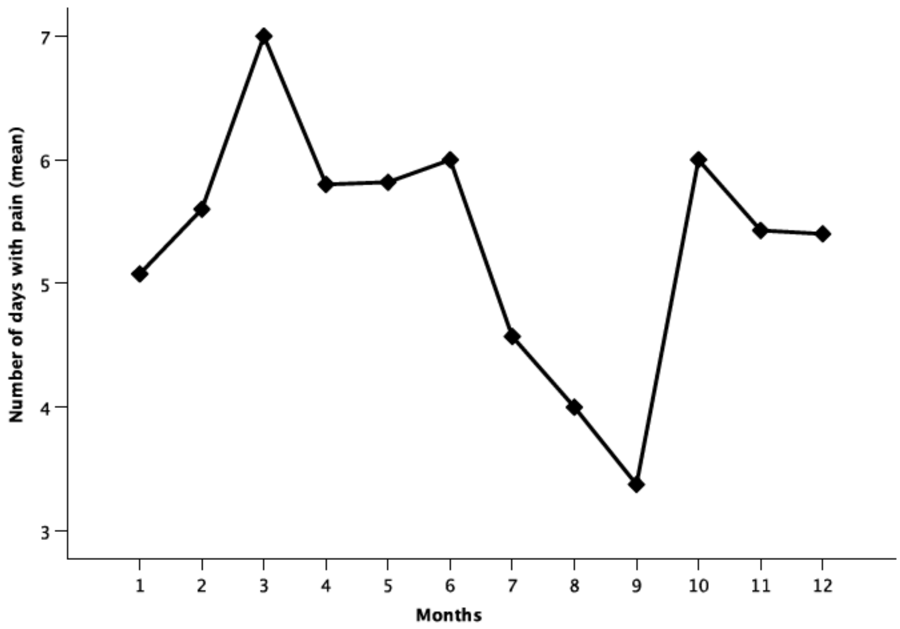

Figure S8: line plot showing mean number of days with pain (outcome) over 12 months follow-up period.

Graph for coefficients paths of LASSO regression (outcome: NDI at 6 months)

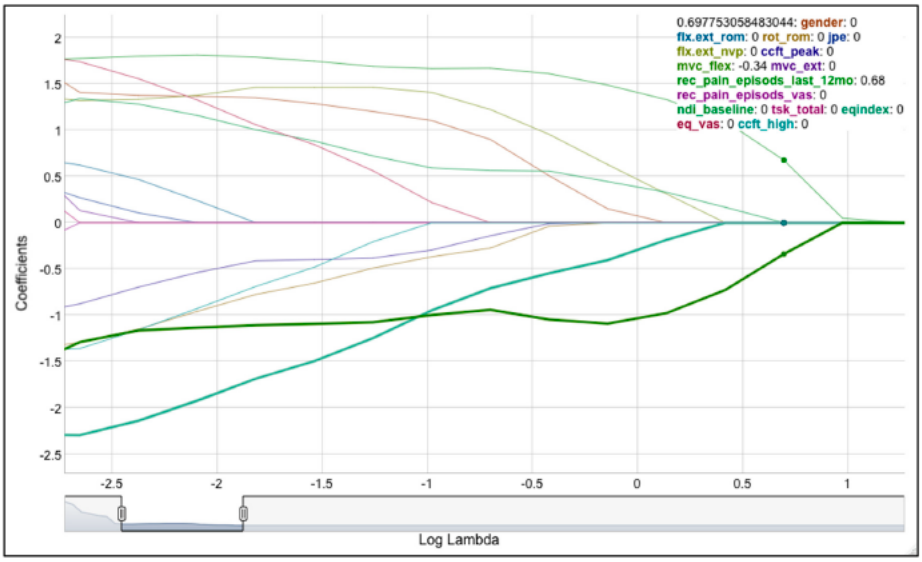

Figure S9: Results of the Least absolute shrinkage and selection operator involving all predictors with Neck Disability Index as an outcome at 6 months.
Legend on the right upper corner showing the included predictors in LASSO where all of them were shrined to Zero, except for mvc_flex = -0.34 and rec_pain_episodes_last_12mo = 0.68 .
mvc_flex: MVC in flexion ; rec_pain_episodes_last_12mo: Previous number of pain episodes in the last 12 months.

Graph for coefficients paths of LASSO regression ((outcome: number of days with pain over the 12-month period)

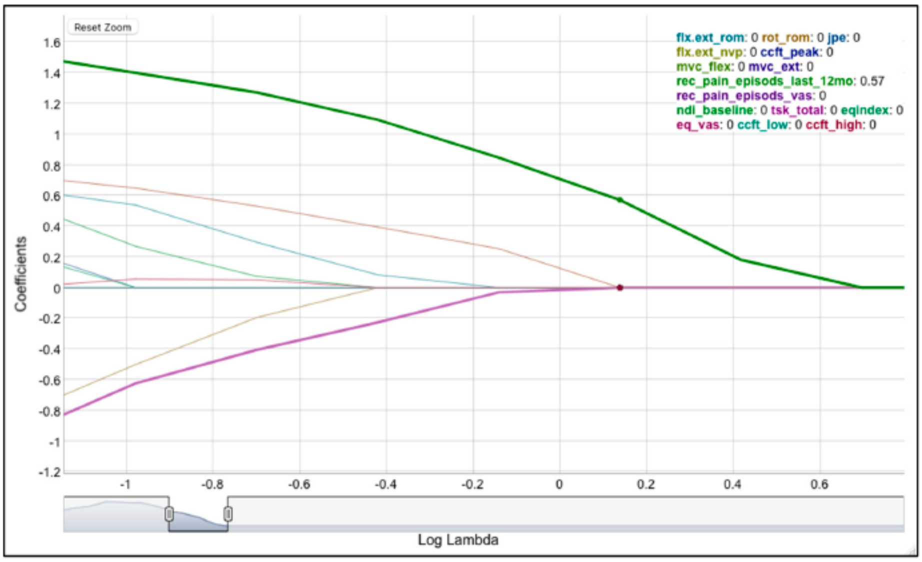

Figure S10: Results of the Least absolute shrinkage and selection operator involving all predictors with days with pain over the 12-month follow-up period as an outcome. Legend on the right upper corner showing the included predictors in LASSO where all of them were shrined to Zero, except for rec_pain_episodes_last_12mo = 0.57 . rec_pain_episodes_last_12mo: Previous number of pain episodes in the last 12 months.

Table S1. STROBE Statement—Checklist of items that should be included in reports of ***cross-sectional studies***

	Item No	Recommendation	Page No
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	1
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	1
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	1-2
Objectives	3	State specific objectives, including any prespecified hypotheses	1
Methods			
Study design	4	Present key elements of study design early in the paper	1
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	3-5
Participants	6	(*a*) Give the eligibility criteria, and the sources and methods of selection of participants	3-4
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	4,7-9
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	5-7
Bias	9	Describe any efforts to address potential sources of bias	NA
Study size	10	Explain how the study size was arrived at	9
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	9
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	9
		(*b*) Describe any methods used to examine subgroups and interactions	NA
		(*c*) Explain how missing data were addressed	10
		(*d*) If applicable, describe analytical methods taking account of sampling strategy	NA
		(*e*) Describe any sensitivity analyses	NA
Results			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	10, 13
		(b) Give reasons for non-participation at each stage	13
		(c) Consider use of a flow diagram	3
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	10
		(b) Indicate number of participants with missing data for each variable of interest	13
Outcome data	15*	Report numbers of outcome events or summary measures	13
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	NA

		(*b*) Report category boundaries when continuous variables were categorized	NA
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	NA
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	NA
Discussion			
Key results	18	Summarise key results with reference to study objectives	15
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	18-19
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	15-18
Generalisability	21	Discuss the generalisability (external validity) of the study results	18-19
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	19

*Give information separately for exposed and unexposed groups.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.

Appendix 4: Alalawi et al. (2022c)

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Contents lists available at ScienceDirect

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Perceived pain and disability but not fear of movement are associated with altered cervical kinematics in people with acute neck pain following a whiplash injury

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ARTICLE INFO

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Kinematics
Smoothness
Velocity
Movement analysis

ABSTRACT

Objectives: To determine if measures of cervical kinematics are altered in people with acute whiplash associated disorders (WAD) and secondarily, to examine whether kinematic variables are associated with self-reported outcomes.

Methods: We recruited people with acute WAD within 15 days after a motor vehicle collision and asymptomatic control participants. All participants performed active neck movements at a self-determined velocity. Maximal range of motion (ROM), peak and mean velocity of movement, smoothness of movement, and cervical joint position error were assessed. Moreover, self-reported measures of perceived pain and disability, pain catastrophising, and fear of movement were obtained.

Results: Sixty people participated: 18 with acute WAD (mean age [SD] 38.7 [12.0]) and 42 as asymptomatic controls (mean age [SD] 38.4 [10.2]). Participants with acute WAD showed significantly decreased ROM in all movement directions ($p < 0.0001$). All participants with acute WAD showed a reduction in the mean and peak velocity of movement in all directions ($p < 0.0001$) and the number of velocity peaks was significantly higher (i.e., reduced smoothness of movement) in those with acute WAD in all directions ($p < 0.0001$). Repositioning acuity following cervical rotation was not significantly different between groups. Neck pain-related disability showed the largest number of significant associations with kinematic features, while fear of movement was not associated with measures of cervical kinematics.

Conclusions: Participants with acute WAD presented with altered cervical kinematics compared to asymptomatic participants. Several measures of cervical kinematics were associated with the level of pain and disability in people with acute WAD but not their fear of movement.

1. Introduction

Whiplash-associated disorders (WAD) are one of the most common injuries associated with motor vehicle accidents, affecting 83% of individuals involved in car collisions (Yadla et al., 2008). A whiplash injury is a source of disability (Carroll et al., 2009a, 2014) that leads to limited work ability (Hoving et al., 2003; Pinfold et al., 2004), and psychological disorders in some patients (Andersen et al., 2016). In western societies, the high prevalence of WAD highlights the need for reliable diagnosis and effective interventions.

One of the most frequently measured physical signs in people with WAD is range of motion (ROM) and several studies report reduced ROM as a common feature in patients with acute (Fernández-Pérez et al., 2012; Kasch et al., 2001; Kumbhare et al., 2005; Sterling et al., 2004)

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and chronic (Woodhouse and Vasseljen, 2008a; Sjölander et al., 2008; Armstrong et al., 2005; Baydal-Bertomeu et al., 2011; Dall'Alba et al., 2001; Madeleine et al., 2004; Grip et al., 2007; Kaale et al., 2007; Klein et al., 2001; Ohberg et al., 2003; Pereira et al., 2008; Prushansky et al., 2006; Puglisi et al., 2004; Shahidi et al., 2012) WAD. In addition to ROM, dynamic kinematic measures of movement such as velocity and the smoothness of movement have also been used previously to quantify changes in cervical kinematics in people following a whiplash injury. The validity of both measures has been established for the assessment of patients with neck pain (Sjölander et al., 2008), and high sensitivity and specificity of the measures have been confirmed (Bahat et al., 2015a). Previous studies report that people with chronic WAD typically move their neck with slower velocity (Ohberg et al., 2003; Vikne et al., 2013; Grip et al., 2008) and perform irregular neck motion (Sjölander et al., 2008). However, despite the functional importance of quick and smooth movements (Takasaki et al., 2013; Tsang et al., 2013; Yan et al., 2000), these kinematic features have not been examined in people with acute WAD.

Besides physical impairments, people often present with a number of relevant symptoms following a whiplash injury, with neck pain being the most frequently reported (Al-Khazali et al., 2020). Initial high levels of pain-related disability (Scholten-Peeters et al., 2003; Williams et al., 2007; Kamper et al., 2008; Carroll et al., 2009b; Walton et al., 2009; Alalawi et al., 2019, 2021), as well as initial higher intensity of neck pain (Williams et al., 2007; Kamper et al., 2008; Carroll et al., 2009b; Walton et al., 2013a), have been identified as predictors of poor outcome following a whiplash trauma (Sarrami et al., 2017; Walton et al., 2013b). Additionally, psychological features such as pain catastrophising (Sullivan et al., 2002a) and fear of movement (Vangronsveld et al., 2008) can be present and both features are associated with poor recovery following a whiplash injury (Shearer et al., 2020). Although the association between measures of cervical kinematics and subjective features such as pain, disability and fear of movement have been examined in people with chronic pain following a whiplash injury or chronic non-specific neck pain (Bahat et al., 2014a; Howell et al., 2012; Treleaven et al., 2016; Waeyaert et al., 2016), there is very limited knowledge on how cervical kinematics are modified in people with acute pain following a whiplash injury and whether any change is associated with subjective complaints.

Understanding how movement is affected in people with acute WAD and how this relates to their symptoms is of relevance as this would prompt specific assessment of kinematic features of neck movement besides ROM (e.g., velocity and smoothness of movement) in people with acute pain and these may become targets for early intervention. Hence, the main objective of this study was to determine if measures of cervical kinematics are altered in people with acute WAD and secondarily, to examine whether kinematic variables are associated with self-reported outcomes, including pain intensity, pain-related disability, fear of movement, catastrophising, and expectations of recovery. We hypothesised that: (i) people with acute WAD will present with altered cervical kinematics including changes in the range, speed and smoothness of their neck movements, and, (ii) that these kinematic variables will be associated with self-reported outcome measures in people with acute WAD. Knowledge from this study could provide preliminary evidence showing that specific movement disturbances exist soon after a whiplash injury, and this may prompt future studies to examine whether movement features are predictive of poor outcome. If movement disturbances prove to be relevant, they could become targets for rehabilitation to improve movement quality aiming to potentially mitigate the transition to chronic pain.

2. Materials and methods

2.1. Study design

An observational case-control study was conducted which was approved by the Ethics Committee of the province of Malaga, Spain (#30052019). This study adhered to the guidelines of the STROBE statement (Strengthening the Reporting of Observational Studies in Epidemiology) (Von Elm et al., 2014), with the checklist available as the supplementary file (S1).

2.2. Participants

A convenience sample of patients with acute WAD were recruited from a single private physiotherapy clinic in Malaga, Spain. They were invited to participate in the study if they were 18 years or older, involved in a recent (previous 15 days) motor vehicle crash, and experienced acute neck pain. Participants were also required to understand written and verbal Spanish. They were excluded if they were categorised as WAD grade IV (spine fractures or dislocations) (Spitzer et al., 1995), or if they lost consciousness during or after their whiplash injury (Cantu, 1992). Participants with a previous history of neck surgery (Crawford et al., 2004), neck injury, malignant spinal disorders, mental disorders (Rosenfeld et al., 2000, 2003), or regular use of analgesic medication prior to the injury due to chronic pain were also excluded.

Electronic clinical records of all consecutive patients attending the clinic were examined manually by a physiotherapist working at the clinic who then invited (either in person or via telephone) eligible people to participate in the study. Once written informed consent was obtained, all participants were asked to complete a baseline self-reported questionnaire and undergo physical testing.

A control group of asymptomatic participants were recruited from a local community at the University of Malaga, Spain through advertisement. Asymptomatic participants for this group were recruited if they have no current neck pain and no history of neck or shoulder pain that required treatment from a healthcare professional.

2.3. Instrumentation

Cervical kinematic data was obtained using a wearable BTS G-WALK® sensor system (BTS Bioengineering, Italy), with a sampling rate of 100 Hz; an Inertial Measurement Unit (IMU) that is composed of a gyroscope, an accelerometer, and a magnetometer. It measures linear and angular characteristics of movement in three-dimensional space. The dimensions for the sensor are 70 × 40 × 18mm, and its mass is 37 g. To collect kinematic data, the sensor was fixed on the participants' forehead using double-sided tape. The data were acquired with the G-Studio software (BTS Bioengineering, Italy). The G-WALK® sensor is a portable system that gives the position and orientation of the head, which allows various kinematic measures to be collected simultaneously including ROM, velocity profiles and the smoothness of motion; making it applicable in clinical practice and for research purposes, compared to other human motion analysis technology. The reliability of G-WALK® sensor have been established, with an Intraclass Correlation Coefficient (ICC) ranging from 0.85 to 0.99 (De Ridder et al., 2019). Similarly, the concurrent validity of the G-WALK sensor for assessing spatiotemporal parameters against a gold standard has been established in healthy participants (De Ridder et al., 2019; Vítečková et al., 2020).

2.4. Testing procedures

Initially, all participants completed baseline self-reported outcomes, prior to physical data collection. Physical testing was then performed by a physiotherapist and consisted of the assessment of cervical kinematics including a measure of proprioception. Each test was carried out with the participated seated in a chair with their arms supported and their feet on the ground. The assessor fixed the sensor on the middle of participant's forehead and calibrated it to zero with the head in a natural position. Participants were then instructed to perform active neck movements as far as possible. The directions of the head movements were performed in the same order among participants.

Firstly, active neck flexion/extension was performed by instructing the participant to look forward, then fully flex and extend their neck continuously without stopping until 5 cycles (trials) were completed. The choice of 5 cycles was chosen to generate a representative sample of data whilst minimising the risk of exacerbating the patients' symptoms. Similar procedures were applied for the active rotation task, whereby the participants performed 5 cycles of continuous right to left rotations. Participants were instructed to perform all movements in a pace that is similar to what they perceive as a normal speed (Sjölander et al., 2008).

Neck proprioception was then assessed and for this, participants performed three repetitions of right and left neck rotation. In each trial, the participants were instructed to memorise a self-selected neutral position (starting position), close their eyes, and perform active head rotation after which they should return to the starting position as accurately as possible. Each movement was repeated three times for both right and left rotation with a rest period of 1 min between each movement.

2.5. Outcome variables

2.5.1. Patient reported outcome measures

Several self-reported outcomes were collected at baseline. To assess neck pain-related disability at baseline, the Neck Disability Index (NDI) (Vernon and Mior, 1991) was used. It consists of 10 items related to daily activities such as reading, lifting, driving, personal care, work, sleeping, and recreation (Vernon and Mior, 1991); each question has five ordinal response options from 0 (no disability) to 5 (complete disability). NDI scores were interpreted as recovered (NDI<8), mild pain and disability (NDI 10–28), moderate/severe pain and disability (NDI>30) (Sterling et al., 2005). The NDI is a valid and reliable measure in individuals with neck pain disorders (Lemeunier et al., 2019). The reliability of Spanish version of the NDI has been established (internal consistency Cronbach's α 0.89; intra-class correlation coefficient 0.98) (Andrade et al., 2008).

Current neck pain intensity was assessed using a Numeric Rating Scale (NRS) which is an 11-point scale range from 0 (no pain) to 10 (worst possible pain). Pain intensity using NRS was also assessed after patients had performed all neck movements testing (NRS-ROM). The reliability of NRS has been established in patients with neck pain (ICC:0.76) (Cleland et al., 2008).

Self-reported outcomes related to pain catastrophising was assessed using the Pain Catastrophising Scale (PCS) which consists of 13-item related to patients' rumination, magnification and helplessness about controlling their pain (Sullivan et al., 1995). It produces an overall score ranging from 0 to 52 with higher scores indicating greater pain catastrophising. PCS has been used to assess patients with WAD (Sterling et al., 2008; Sullivan et al., 2002b), and its reliability and validity have been established (Sullivan et al., 1995). The Spanish version of PCS was used in this study (internal consistency Cronbach's α 0.79; test-retest reliability 0.84) (García Campayo et al., 2008).

The Tampa Scale of Kinesiophobia (TSK-11) (Roelofs et al., 2007) was used to assess fear of movement or injury during activities. It consists of 11-items producing a range score from 11 to 44 with (higher scores representing higher fear of movement). Scores greater than 37 is considered a high degree of fear of movement (Vlaeyen et al., 1995). The reliability and validity of TSK-11 have been established (Woby et al., 2005). The Spanish version of TSK was used in this study (internal consistency Cronbach's α 0.81 for people with acute pain) (Gómez-Pérez et al., 2011).

A single question was asked to determine recovery expectations among patients; "In your opinion, how likely is it that you will be fully recovered with no persistent sequelae?" (Elrud et al., 2016). Scores ranged between 0 ("not likely") and 10 ("very likely") to indicate how likely he/she will completely recover (Holm et al., 2008).

2.6. Objective outcome measures (cervical kinematics and proprioception)

Data were analysed in Matlab (Mathworks Matlab, 2019b). Signals were low pass–filtered (cut-off frequency of 10Hz; order: 10), as used previously (Sjolander et al., 2008). The start and end of the movement were defined as the time when the peak velocity passed the threshold of 5%, as used previously (Sjolander et al., 2008).

Maximum neck ROM (°) was defined as the maximum range achieved during each repetition of flexion, extension, right and left rotation. The mean value of the five repetitions for each direction was calculated and included in the analysis of this study.

Mean velocity (V*mean* [°/s]) was determined as the mean angular velocity achieved over the five repetitions for each movement direction. The average of the five values was included in the analysis for each movement direction.

Peak velocity (V*peak* [°/s])) refers to the maximal velocity value for each movement; the average of the five repetitions were included in the analysis for each movement direction.

Number of velocity peaks (NVP [n]) refers to the number of times that the acceleration curve crossed zero. The average NVP that occurred across the five repetitions were combined and included in the analysis for each movement direction.

Joint Position Error (JPE [°]) refers to the difference in degrees between the participants head position upon repositioning and the start location. The mean value of the three repetitions for each direction was calculated and included in the analysis.

2.7. Statistical analyses

Descriptive statistics between groups were performed for participant demographics, self-reported questionnaires, cervical kinematic features, and proprioception. The normality of data distribution for self-reported and objective outcomes was assessed using the Shapiro-Wilk Test. Based on the normality test, differences between groups were assessed using the independent *t*-test. Other variables such as mean velocity in extension and right rotation, peak velocity in flexion and rotations, NVP in flexion, extension, and right rotation, and JPE task in left rotation were not normally distributed and differences between groups were assessed using the Mann-Whitney *U* Test.

Bivariate correlations between self-reported outcome (NRS, NRS-ROM, NDI, TSK, PCS, recovery expectations) and objective measures were performed. Pearson's correlation coefficient was used if data was normally distributed, or Spearman's correlation coefficient if data were not normally distributed. Analyses were performed using SPSS 26.0 (IBM Corp.,Armonk, NY, USA). Group differences were considered significant at the $p < 0.05$.

2.8. Sample size

Because no previous study has investigated cervical kinematics in individuals with acute WAD, an a priori sample size could not be calculated.

3. Results

The baseline demographic characteristics of included participants in each group with their scores for the self-reported measures are summarised in Table 1. Results were analysed from a sample of 18 patients with acute WAD (14 women, 4 men, mean age 38.7 ± 12.0, mean BMI 25.2 ± 6.0), and 42 asymptomatic controls (33 women, 9 men, mean age 38.4 ± 10.2, mean BMI 23.0 ± 3.8). No significant differences were observed between groups with regards to age (p 0.45), gender (p 0.95), or BMI (p 0.17). Self-reported questionnaires indicated that the patients presented with moderate/severe neck disability (mean NDI: 32.8 ± 7.5, range 17–44), high neck pain intensity (mean NRS: 6.9

Table 1
Baseline characteristics.

	Groups				p-value
	Acute (N 18)		Controls (N 42)		
	Mean (SD)	Median (IQR)	Mean (SD)	Median (IQR)	
Age (years)	38.7 (12.0)	38.0 (18.0)	38.4 (10.2)	38.5 (18.0)	0.45 [a]
Gender (women/men), n	14/4		33/9		0.95 [b]
BMI (kg/m^2)	25.2 (6.0)	23.2 (7.0)	23.0 (3.8)	21.6 (3.4)	0.17 [c]
NDI (0–50)	32.8 (7.5)	35.0 (11.0)			
NRS (0–10)	6.9 (1.9)	7.0 (3.0)			
NRS-ROM (0–10)	7.3 (1.6)	7.0 (2.0)			
PCS (0–52)	21.4 (19.8)	13.0 (41.0)			
TSK (11–44)	33.4 (9.6)	37.0 (14.0)			
Recovery expectations (0–10)	8.0 (2.1)	8.5 (3.0)			

Abbreviations.
SD: standard deviation; IQR: interquartile range; NDI: neck disability index; NRS: numerical rating scale; NRS-ROM: neck pain taking immediately after neck motion tasks; PCS: pain catastrophizing scale; TSK: tampa scale of kinesiophobia.
[a] Independent T-Test.
[b] Pearson's Chi-squared test.
[c] Mann-Whitney Test.

± 1.9, range 3–10), pain catastrophising (mean PCS: 21.4 ± 19.8, range 0–52), moderate fear of movement (mean TSK: 33.4 ± 9.6, range 11–44), but were mostly optimistic about their full recovery (mean recovery expectations: 8.0 ± 2.1, range 3–10).

3.1. *Cervical kinematics*

Summary statistics and differences between groups for maximal neck ROM, mean velocity, peak velocity, and JPE for both groups are presented in Table 2.

Compared to the control group, results from the independent *t*-test showed that patients with acute WAD presented with a significantly lower maximal cervical ROM in all movement directions ($p < 0.001$). For those with acute WAD, their neck ROM was approximately 37% less in flexion, 43% less in extension, 27% less in right rotation, and 39% less in left rotation, compared to the ROM of the healthy participants.

Similarly, significant differences between groups were also observed for the mean and peak velocity where participants with acute WAD moved their neck slower than the asymptomatic participants in all directions ($p < 0.001$). Mean and peak velocity in the sagittal plane (neck flexion and extension) was slower than in the transverse plane of movement (neck rotation). Those with acute WAD had, on average, 30% of the mean velocity of asymptomatic participants during active flexion and extension, compared to 32% in right and left rotation.

The NVP was significantly higher in those with acute WAD in all directions ($p < 0.001$), indicating that those with acute neck pain move their neck with more irregular movement. The movements with highest NVP were extension (mean difference 42.3) and flexion (mean difference 34.8), followed by left rotation (mean difference 34.4) and right rotation (mean difference 30.3).

Finally, head repositioning acuity measured as the JPE on return to neutral following active cervical rotation was not significantly different between groups in either right (mean difference 0.2; p 0.39) or left rotations (mean difference 0.7; p 0.17).

3.2. *Correlation between subjective reports and cervical kinematics*

Table 3 presents correlations between self-reported outcome variables and kinematic measures in those with acute WAD. NDI was the self-reported measure that showed the greatest number of significant associations with kinematic measures (12 out of 18) (all p values <

Table 2
Summary statistics and differences between groups.

Kinematic Measures	Groups				Mean Diff	95% Confidence Interval of the Difference		Sig. (2-tailed)
	Acute		Controls					
	Mean (SD)	Median (IQR)	Mean (SD)	Median (IQR)		Lower	Upper	
Flexion								
ROM (°)	27.7 (15.0)	24.7 (24.3)	44.1 (12.7)	44.1 (21.1)	16.4	24.0	8.8	**<0.001**
Vmean (°/s)	15.7 (9.7)	13.2 (14.7)	55.3 (14.6)	54.4 (19.7)	39.6	47.5	31.7	**<0.001**
Vpeak (°/s)	41.3 (23.7)	35.1 (40.0)	107.2 (28.3)	104.5 (33.2)	65.8	81.4	50.3	**<0.001** [a]
NVP (n)	49.0 (28.8)	47.0 (47.4)	14.2 (6.4)	12.4 (8.8)	34.8	25.5	44.1	**<0.001** [a]
Extension								
ROM (°)	29.7 (12.2)	26.9 (19.8)	51.9 (11.7)	52.6 (16.9)	22.2	28.9	15.5	**<0.001**
Vmean (°/s)	17.6 (12.4)	12.6 (20.3)	55.0 (12.7)	57.1 (14.6)	37.3	44.6	30.1	**<0.001** [a]
Vpeak (°/s)	44.3 (24.5)	40.3 (41.9)	108.1 (24.6)	103.8 (30.8)	63.8	78.1	49.6	**<0.001**
NVP (n)	57.5 (32.8)	59.0 (55.7)	15.2 (6.8)	13.5 (8.0)	42.3	31.7	52.8	**<0.001** [a]
Right Rotation								
ROM (°)	42.9 (13.7)	44.8 (24.2)	59.0 (14.4)	60.6 (23.7)	16.1	24.4	7.9	**<0.001**
Vmean (°/s)	26.1 (14.9)	23.3 (16.0)	83.2 (36.3)	76.4 (43.1)	57.1	75.4	38.8	**<0.001** [a]
Vpeak (°/s)	71.2 (35.2)	64.8 (52.5)	186.9 (65.2)	171.2 (101.3)	115.7	149.5	82.0	**<0.001** [a]
NVP (n)	42.9 (19.5)	40.5 (25.4)	12.6 (6.3)	11.5 (9.6)	30.3	23.6	37.1	**<0.001** [a]
JPE (°)	3.4 (2.1)	3.3 (3.2)	3.2 (2.1)	3.2 (2.7)	0.2	1.1	1.4	0.39
Left Rotation								
ROM (°)	29.4 (8.7)	30.0 (9.5)	47.9 (15.3)	47.5 (22.9)	18.5	26.4	10.5	**<0.001**
Vmean (°/s)	25.1 (16.2)	19.3 (18.2)	77.1 (26.5)	73.7 (30.9)	52.0	65.8	38.1	**<0.001** [a]
Vpeak (°/s)	72.6 (39.1)	56.1 (48.0)	180.3 (70.3)	168.4 (82.4)	107.7	144.2	71.2	**<0.001**
NVP (n)	47.3 (24.5)	40.2 (37.0)	12.9 (5.7)	11.2 (7.5)	34.4	26.2	42.6	**<0.001**
JPE (°)	3.8 (2.4)	3.1 (3.3)	3.1 (2.6)	2.5 (2.6)	0.7	0.8	2.2	0.17 [a]

Abbreviations.
SD: standard deviation; IQR: interquartile range.
Mean diff: mean difference; ROM: range of motion; Vmean: mean velocity; Vpeaks: mean of peaks velocity; NVP: number of velocity peaks; JPE: joint position error.
[a] Z scores from Mann-Whitney Test.

Table 3
Correlation results between self-reported measures and neck kinematic measures of patients with acute WAD.

Kinematic Measures	NRS	NRS-ROM	NDI	TSK	PCS	Recovery Expectations
Flexion						
ROM (°)	**0.53***	**0.52***	0.33	0.06	0.36	0.13
Vmean (°/s)	0.35	0.37	**0.62****	0.26	**0.46***	0.05
Vpeak (°/s) [a]	**0.45***	**0.43***	**0.70****	0.22	**0.52***	0.06
NVP (n) [a]	0.09	0.05	**0.44***	0.37	0.13	0.11
Extension						
ROM (°)	**0.60****	**0.50***	**0.66****	0.25	**0.68****	0.21
Vmean (°/s) [a]	0.33	0.32	**0.58****	0.36	**0.43***	0.07
Vpeak (°/s)	0.27	0.26	**0.55***	0.36	**0.53***	0.1
NVP (n) [a]	0.16	0.19	**0.45***	0.34	0.32	0.05
Right Rotation						
ROM (°)	0.39	0.33	**0.46***	0.05	0.02	**0.48***
Vmean (°/s) [a]	0.23	0.22	**0.48***	0.02	0.17	0.14
Vpeak (°/s) [a]	0.17	0.11	**0.44***	0.13	0.1	0.23
NVP (n) [a]	0.14	0.15	**0.42***	0.09	0.21	0.01
JPE (°)	0.22	0.17	0.04	0.22	0.24	**0.53***
Left Rotation						
ROM (°)	0.12	0.04	0.13	0.13	0.21	0.21
Vmean (°/s)	0.16	0.18	**0.52***	0.31	0.34	0.1
Vpeak (°/s) [a]	0.26	0.23	0.38	0	0.32	0.03
NVP (n)	0.09	0.1	0.32	0.29	0.23	0.17
JPE (°) [a]	0.15	0.18	0.14	0.22	0.22	0.2

Pearson product moment correlation coefficients (r) are presented, unless something else is specified.
Significant correlation was indicated in bold ($P < 0.05$ (*) or $P < 0.001$ (* *)).
Abbreviations.
NDI: neck disability index; NRS: numerical rating scale; NRS-ROM: neck pain taking immediately after neck motion tasks; PCS: pain catastrophizing scale; TSK: tampa scale of kinesiophobia.
ROM: range of motion; Vmean: mean velocity; Vpeaks: mean of peaks velocity; NVP: number of velocity peaks; JPE: joint position error.
[a] Spearman's correlation.

0.05). NDI was significantly correlated with mean velocity of movement in all directions (coefficients range from −0.48 to −0.62), with peak velocity in flexion, extension, and right rotations (r range −0.44 to −0.70), with NVP in flexion, extension, and right rotations (r range 0.42 to 0.45), and with cervical ROM in extension and right rotation (r range −0.46 to −0.66). In contrast, the level of fear of movement measured via the TSK was not correlated with any of the kinematic measures. Recovery expectations largely did not correlate with the measures of cervical kinematics whereas the degree of catastrophising did correlate with the peak and mean velocity in flexion and extension as well as the ROM of extension.

4. Discussion

This study quantified cervical kinematic features in people with acute WAD and assessed their association with self-reported outcomes of pain, disability, catastrophising and fear of movement. In support of our hypothesis, the results demonstrate that soon after a whiplash injury, people present with restricted, slower and irregular movements in all directions compared to asymptomatic controls. Higher neck pain and disability in people with acute WAD is significantly associated with several kinematic features, including movement velocity and range. However, fear of movement was not associated with any of the cervical kinematic measurements. These findings suggest that pain and disability dictate changes in neck movement soon after injury, although causality cannot not be established at this stage.

4.1. Range of movement

This study found that maximal ROM was significantly lower in all directions in patients with acute WAD compared to asymptomatic controls. This finding is consistent with previous studies which reported restricted ROM in patients with acute (Fernández-Pérez et al., 2012; Kasch et al., 2001; Kumbhare et al., 2005; Sterling et al., 2004) and chronic (Woodhouse and Vasseljen, 2008a; Sjölander et al., 2008; Armstrong et al., 2005; Baydal-Bertomeu et al., 2011; Dall'Alba et al., 2001; Madeleine et al., 2004; Grip et al., 2007; Kaale et al., 2007; Klein et al., 2001; Ohberg et al., 2003; Pereira et al., 2008; Prushansky et al., 2006; Puglisi et al., 2004; Shahidi et al., 2012) WAD, despite methodological differences. This study also found that restricted ROM was associated with pain intensity and pain-related disability, as observed in another study (Fernández-Pérez et al., 2012). This could indicate that patients with higher of pain and disability tend to move their neck less likely due to the intensity of their pain. Reduced neck motion could be interpreted as protective mechanism to minimize the potential damage to the neck in agreement with the pain-adaptation model (Lund et al., 1991).

4.2. Mean and peak velocity of neck movement

To our knowledge there are no studies that have measured the velocity of movement in patients with acute WAD. In the current study, the average mean and peak velocity during neck flexion, extension, and rotations were lower in those acute WAD compared to the control group. We also observed that the mean velocity of neck movement was negatively associated with neck pain-related disability and this was the case for all movement directions, that is, the greater the pain-related disability, the slower the neck moves. Given the cross-sectional nature of our data, we cannot draw firm conclusions regarding a cause-effect relationship. Interestingly, studies have reported reduced velocity of neck movement in patients with chronic WAD (Ohberg et al., 2003; Vikne et al., 2013; Grip et al., 2008) and chronic idiopathic neck pain (Sjölander et al., 2008; Tsang et al., 2013; Bahat et al., 2010; Röijezon et al., 2010) and therefore it would be relevant to investigate whether early signs of slow neck movements are predictive of the transition to chronicity.

4.3. Cervical joint position error

The current study found no significant differences between groups with regards to cervical proprioception measured as the JPE. Several studies have evaluated JPE in patients with either acute (Sterling et al.,

2003) or chronic (Sjölander et al., 2008; Armstrong et al., 2005; Grip et al., 2007; Feipel et al., 2005; Heikkilä and Wenngren, 1998; Kristjansson et al., 2003; Treleaven et al., 2003; Woodhouse and Vasseljen, 2008b) WAD, yet with inconclusive results. Sterling et al. (2003) assessed JPE in patients with acute WAD presenting with moderate/severe disability which is similar to the level of disability of the current sample. The study found that patients with acute WAD and higher disability presented with a larger error of 2.2° and 1° compared to the healthy controls following right (significant differences) and left rotations (non-significant differences), respectively. We suspect that the lack of significance in the current studies is due to methodological differences or the variability among participants. We did not account for the presence of dizziness in our study, however, given that people with chronic WAD presenting with dizziness tend to show greater deficits in sensorimotor control (Treleaven, 2011), subgrouping by the presence or absence of dizziness should be considered in future studies in acute WAD.

4.4. *Smoothness of neck movement*

Patients with acute WAD moved their neck with a high number of velocity peaks in all directions which indicates that their movements were interrupted frequently and were not as smooth as that observed in asymptomatic controls. Previous work has shown that people with chronic neck pain either from traumatic or non-traumatic causes, display deficits in the smoothness of neck movement (Bahat et al., 2015a). While the underlying mechanism of irregular movement in patients with acute WAD remain unclear, other studies in patients with chronic WAD suggested that such a pattern might be a consequence of motor control disturbances (Sjölander et al., 2008; Grip et al., 2008). Therefore, the underlying mechanism of irregular movement soon after a whiplash injury should be investigated in further studies by measuring electromyography in addition to cervical kinematics.

4.5. *Association between self-reported measures and cervical kinematic features*

A secondary aim of this study was to determine the relationship between self-reported measures and measures of cervical kinematic features in people with acute WAD. This study revealed that pain catastrophising is present soon after a whiplash injury. Findings from this study also indicated that the reduced velocity of movement and restricted motion during cervical extension were negatively associated with pain catastrophising. This interaction between the adapted motor behaviour (e.g., restricted motion and reduced velocity of movement) and catastrophising may feed into fear-avoidance model (Vlaeyen and Linton, 2000). It could be indicated that patients with acute WAD may restrict their cervical movement and slow down their motion as a protective and guarding mechanism to avoid excessive force and loading, hence decreasing neck pain. This notion is supported by a study conducted in people with low back pain, where a negative association between the velocity of trunk movement and pain catastrophising was established (Vaisy et al., 2015). However, in the current study fear of movement was not associated with cervical kinematic features. One potential explanation for this could be the large variation in TSK scores among our participants with acute WAD with scores ranging from the lowest possible score (11) to the highest (44) on the TSK scale. In contrast, kinesiophobia, assessed via the TSK, was significantly associated with cervical kinematic features (ROM, velocity, and smoothness of movement) in people with chronic neck pain of traumatic and non-traumatic origin (Bahat et al., 2014b). These findings were also confirmed in people with chronic and recurrent neck pain, where higher fear of movement was associated with altered quality of movement (Devecchi et al., 2022). It may be that during the acute phase, neck movement is more influenced by pain rather than fear or other psychological features. Notably, the NDI was the self-reported measure that showed the greatest number of significant associations with kinematic measures (12 out of 18).

4.6. *Methodological considerations*

A limitation of this study is the relatively small sample size of those with acute WAD which might reduce the generalisability of study findings. Therefore, the findings from this study should be treated with caution due to the small number of observations. However, despite this, we were able to determine significant differences between groups for all cervical kinematics, apart for cervical proprioception. Additionally, a post-hoc power analysis (GPower 3.1.9.6, Kiel University, Germany) indicated that the current sample size and the observed effect size of 1.14 for the main outcome (neck flexion ROM) yielded a power of 98% at an alpha level of 0.05, supporting the sample size of the study. A further limitation in this study is that pre-existing conditions (e.g., pre-existing pain, restricted mobility) in patients with acute WAD prior to their inception were not considered. Nevertheless, these preliminary results prompt future longitudinal studies to evaluate the potential prognostic role that cervical kinematic measures may have in the transition from acute to chronic WAD.

4.7. *Clinical implications*

The current study indicated that patients with acute WAD moved their neck with slower and irregular movement in all directions. These findings are also evident in people with chronic neck pain either of traumatic or non-traumatic origin (Bahat et al., 2010, 2015b; Gregori et al., 2008). Rehabilitation programmes typically focus on improving neck ROM and there has been little emphasis on addressing other kinematic features such as reduced movement velocity, control, or quality of movement (Jull, 2011). Evidence from people with chronic neck pain showed significant improvement in NDI, ROM, and velocity of movement following kinematic training with and without the use of an interactive virtual reality device and the effects were sustained for up to three months post-intervention (Bahat et al., 2015b). The intervention consisted of 4–6 kinematic training sessions involving active and quick head movement as well as fine head movement control performed over a period of 5 weeks. One potential explanation for such improvement in pain and disability is the improvement in the person's capacity to move the head further, faster, and more precisely (Bahat et al., 2015b). It could be inferred that such an intervention could also be helpful also for people with acute WAD. Thus, future studies should evaluate the value of kinematic training in the acute stage to enhance the velocity and smoothness of neck movements. Given that these features are associated with higher pain and disability, then addressing movement dysfunction may help to alleviate pain and even minimize the transition to chronicity. Although, longitudinal studies are required to corroborate this statement.

5. Conclusion

People with acute WAD present with restricted, slower and irregular neck movements. Changes in neck movement were associated with higher neck pain intensity and disability, but not fear of movement.

Declaration of competing interest

The authors have no competing interests to report.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.msksp.2022.102633.

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Appendix 5: Alalawi et al. (2022d)

Are Measures of Physical Function of the Neck Region Associated With Poor Prognosis Following a Whiplash Trauma?

A Systematic Review

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Objective: The objective of this study was to synthesize the current evidence regarding the predictive ability of measures of physical function (PF) of the neck region and perceived PF on prognosis following a whiplash injury.

Materials and Methods: Electronic databases were searched by 2 independent reviewers up to July 2020, including MEDLINE, EMBASE, CINAHL, PsycINFO, Scopus, and Web of Science as well as gray literature. Eligible studies were selected by 2 reviewers who then extracted and assessed the quality of evidence. Observational cohort studies were included if they involved participants with acute whiplash-associated disorders (WAD), followed for at least 3 months postinjury, and included objective measures of neck PF or self-reported measures of PF as prognostic factors. Data could not be pooled and therefore were synthesized qualitatively.

Results: Fourteen studies (13 cohorts) were included in this review. Low to very low quality of evidence indicated that initial higher pain-related disability and higher WAD grade were associated with poor outcome, while there was inconclusive evidence that neck range of motion, joint position error, activity of the superficial neck muscles, muscle strength/endurance, and perceived functional capacity are not predictive of outcome. The predictive ability of more contemporary measures of neck PF such as the smoothness of neck movement, variability of neck motion, and coactivation of neck muscles have not been assessed.

Discussion: Although initial higher pain-related disability and higher WAD grade are associated with poor outcome, there is little evidence available investigating the role of neck PF on prognosis following a whiplash injury.

Key Words: whiplash, physical factors, prognosis, neck pain, trauma

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A.A. is a PhD student with D.F. as a lead supervisor and A.G. and A.L.-S. as co-supervisors. A.A.: drafted the initial review with guidance from D.F. at all stages. M.M.: was the second reviewer. M.S., A.L.-S., and A.G.: provided feedback on manuscript drafts and all authors approved the final version for publication. D.F.: is guarantor.

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Whiplash injury is one of the most common injuries caused by a motor vehicle accident.[1,2] It leads to the development of a variety of clinical symptoms commonly known as whiplash-associated disorder (WAD).[3] WAD is a common source of disability[4,5] that may lead to limited work ability, frustration, depression, anger, fatigue, and restricted participation in recreational activity.[6,7] WAD pose a substantial socioeconomic burden,[8] with annual costs of ~£3 billion to the UK economy alone.[9] There is a high transition rate from acute to chronic WAD[5,10,11] and limited evidence of effective interventions for chronic WAD.[12,13] Therefore, mitigation of the transition from acute to chronic WAD is a priority that could be achieved through early identification of factors that increase the risk of developing persistent symptoms[14] and early targeted interventions.

Besides pain and pain-related disability, people with WAD are known to present with objective changes in physical function (PF) of the neck.[15,16] This includes increased activation of the superficial neck flexors,[17] reduced maximum angular velocity of neck movements,[15,16] and reduced smoothness of neck movement.[16] Moreover, other changes such as increased repositioning error,[18] reduced conjunct motion,[19] and changes in deep neck muscle activation[20] have also been observed in patients with chronic WAD. Of relevance, studies in acute WAD have revealed early changes in motor behavior[17] that may persist even after the acute phase[17,20] suggesting that these factors could play a role in the transition to chronicity.

Several systematic reviews have aimed to identify prognostic factors associated with poor outcome following a whiplash injury.[5,10,21–31] Initial high levels of pain-related disability,[5,10,26,28,29] as well as initial higher intensity of neck pain,[5,10,21,28] have been identified as consistent predictors of poor outcome. Yet very few systematic reviews have examined the predictive ability of physical features on poor outcome following a whiplash injury. Of those conducted, the features examined were mostly cervical range of motion (ROM).[10,23,28,29,31] The predictive ability of changes in the activity of the superficial neck muscles was also assessed in one review.[23] Given that this review was published 8 years ago, it is likely that new literature has emerged that could strengthen the conclusions on the role of physical factors in prognosis following a whiplash injury. In addition, other measures of neck function such as the variability of neck movement or the smoothness of neck movement have not been considered in any existing review.

Therefore, the aim of this review was to update and summarize the role of objective measures of neck PF or self-reported measures of PF that have been used in prognostic research following a whiplash injury and to synthesize and assess the overall quality of evidence on the predictive ability of these factors on neck pain and disability in individuals following a whiplash injury.

MATERIALS AND METHODS

This review was planned according to the guidelines for conducting prognostic reviews[32] and reported according to the guidelines from Preferred Reporting Items for Systematic reviews and Meta-Analyses (PRISMA) 2020 statement,[33] the Cochrane Back Review Group guidelines,[34] and the Cochrane Handbook.[35] The protocol for this review was registered prospectively on PROSPERO (International Prospective Register of Systematic Reviews) (CRD42019122559) on the 05/08/2019 and was published in advance.[36]

Eligibility Criteria

The PECOT framework (P = population; E = exposure; C = comparator; O = outcome; T = Type of study) was utilized to inform the inclusion criteria of this review.[35] The comparator component was not considered in this review, given the nature of the research objective.

Population

Studies were required to include participants aged above 16 years old with acute WAD (< 6 wk) due to a motor vehicle crash or sports injury and classified as grade I, II, or III on the Quebec Task Force (QTF) classification.[3] Moreover, primary studies needed to include at least a 3-month follow-up.

Exposure

Due to the inconsistency in the definition of PF in the field of WAD, PF was included in this review if it involved a feature of neck PF that can be measured objectively, for example, joint position error (JPE), onset and amplitude of muscle activation, range, quality and velocity of neck movement, neck muscle strength and endurance, neck muscle fatigue, and balance. We also included self-reported measures of physical functioning, among others, physical component of the 36-Item Short-Form Survey (SF-36)[37] and the Neck Disability Index (NDI)[38] were selected. In addition, the QTF Classification of WAD was included since neck ROM is considered within the grading.

Outcome

The primary outcome of interest was the NDI[38] measured at least at a 3-month follow-up. Other validated outcomes such as pain intensity, psychological status, health-related quality of life, self-rated recovery, and functional recovery were considered as secondary outcomes.

Type of Study

Primary studies were included if they had an observational design and if they were published in English.

Exclusion Criteria

Studies were excluded if they included patients with previous neck or shoulder surgery, previous cervical pain that warranted treatment from a health care practitioner, or combined participants with WAD with patients reporting other musculoskeletal injuries.

Search Strategy

Several electronic databases were searched from 1995 to July 2020, including Medline (OVID), EMBASE (OVID), Cumulative Index to Nursing and Allied Health Literature (CINAHL), PsycINFO (OVID), Scopus, and Web of Science. In addition, potential studies were searched in gray literature through ZETOC database, complemented by a hand search of reference lists of relevant published reviews.[5,10,21 31] A complete search strategy example was provided in the published protocol.[36]

Study Selection

Eligible studies were selected by 2 reviewers (A.A., M.M.) who independently screened titles and abstracts of all retrieved studies against the predetermined eligibility criteria after removing duplicates. Eligible full-text studies were screened by the same reviewers, and any disagreement between the reviewers in the study selection process was resolved by discussion.

Data Extraction

Both reviewers extracted the data from a small number of eligible studies (n = 5) independently.[32] Due to the similarity of extracted data between the reviewers, the remainder of the eligible studies were extracted by the first reviewer (A.A.), and then their accuracy was confirmed by a second reviewer (M.M.). A third reviewer (D.F.) was available to mediate any disagreement in data extraction.

Data Items

Extracted data were authors and year of publication, study location, study setting, time since the crash, sample size, demographic characteristics, interventions received, prognostic factors, outcomes of interest, length of follow-up, methods for statistical analysis, and findings.

Risk of Bias

The Quality In Prognostic Studies (QUIPS) tool[39] was used to evaluate the risk of bias of the included studies (Supplementary File S1, Supplemental Digital Content 1, http://links.lww.com/CJP/A850). Two steps of assessment were used to facilitate the decision. Initially, each of the 6 domains in the QUIPS tool (study participation, study attrition, prognostic factor measurement, outcome measurement, study confounding, statistical analysis and reporting) was judged either as low, moderate, or high risk of bias, based on the number of fulfilled items under each domain. The chosen rating was judged using equally spaced cutoffs of 0% to 33% (high), 34% to 66% (moderate), and 67% to 100% (low). For example, if 5 of the 6 items of the first QUIPS domain (study participation) were fulfilled and reported, this domain was rated as low risk of bias, as 83%

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of items for this domain were reported. Finally, to assess the overall study quality, we classified a study to have a low risk of bias if 5 of the domains were low and none had high risk, a moderate risk of bias if a maximum of 2 domains were judged as moderate risk and the others were low risk and a high risk of bias if any domain was judged as high risk or had > 3 moderate domains.[40] The items under each domain were tailored to this review. Two reviewers (A.A., M.M.) assessed the risk of bias of each study independently. Any disagreement between the assessors in the assessment of risk of bias was resolved by discussion. A third assessor (D.F.) was available if needed.

Quality of Evidence

Using the modified GRADE framework,[41] the overall level of evidence for a prognostic factor across studies was assessed by considering 6 elements including the phase of the investigation, study limitations, inconsistency, indirectness, imprecision, and publication bias.[42,43] More emphasis was placed on the phase of investigation with phase II and III explanatory studies rated as a high level of evidence[42] and phase I explanatory studies rated as a moderate level of evidence. Following this, the evidence was downgraded based on the GRADE criteria as described before.[42] *Study limitations* was downgraded if most evidence came from studies with a moderate or high risk of bias. *Inconsistency* for a prognostic factor was downgraded if the association between the factor and an outcome showed a variation in the direction (from significant to nonsignificant) with no or minimal confidence interval overlap. In addition, it was downgraded if a prognostic factor was only presented in 1 study. With regards to *indirectness*, this element was downgraded if several tools were detected to measure a prognostic physical factor. Population and relevant outcomes were not considered in judging this domain as they were specified in the inclusion criteria.[25] *Imprecision* was downgraded if studies were unpowered, the width of confidence interval appeared excessively wide, or fewer number of studies and/or participants. Finally, *publication bias* was downgraded for all prognostic factors in this review due to the small number of studies for each potential physical factor and the presence of publication bias in prognostic research.[44]

The level of evidence was assessed by 2 reviewers (A.A., M.M.) and rated as high, moderate, low, or very low. Any disagreement between the assessors in using GRADE was resolved by discussion. A third assessor (D.F.) was available if needed.

Data Synthesis and Analysis

Even though combining quantitative data from the included studies was planned in advance, a meta-analysis was not feasible along with the assessments of heterogeneity,

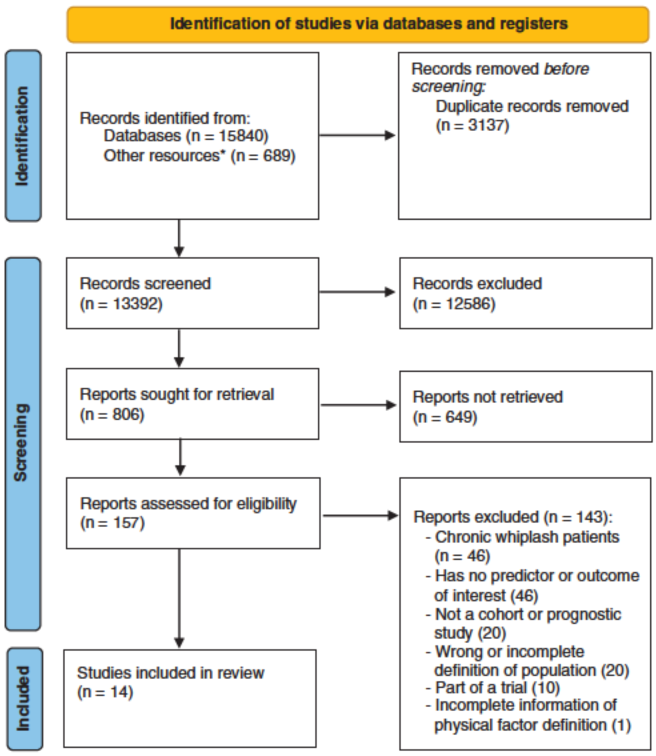

FIGURE 1. Preferred Reporting Items for Systematic reviews and Meta-Analyses (PRISMA) 2020 flow diagram. *Other resources that were identified searching the gray literature and hand search of reference lists of relevant published reviews.

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TABLE 1. Risk of Bias of Included Studies Assessed Using the Quality In Prognostic Studies (QUIPS) Tool

	QUIPS Domains						
References	Study Participation	Study Attrition	Prognostic Factor Measurement	Outcome Measurement	Study Confounding	Statistical Analysis and Reporting	Overall Risk of Bias
Kasch et al[54]	Low	High	Low	Moderate	Low	High	High
Hartling et al[57]	Low	Moderate	Low	Moderate	High	Moderate	High
Kyhlback et al[50]	Low	Moderate	Low	Low	Low	Moderate	Moderate
Sterner et al[56]	Low	Moderate	Low	Moderate	Low	Moderate	High
Gun et al[55]	Moderate	High	Low	Moderate	Low	Low	High
Sterling et al[52]	Low	Moderate	Low	Low	Low	Moderate	Moderate
Atherton et al[45]	Low	Moderate	Low	Low	Low	Low	Low
Berglund et al[47]	Low	Low	Low	Low	Low	Moderate	Low
Sterling et al[51]	Low	Moderate	Low	Low	Low	Moderate	Moderate
Kivioja et al[46]	Low	Moderate	Low	Low	Low	Low	Low
Cobo et al[58]	Low	High	Low	Low	High	Moderate	High
Sterling et al[48]	Low	Moderate	Low	Low	Low	Low	Low
Ritchie et al[49]	Low	Moderate	Low	Low	Low	Low	Low
Hours et al[53]	Low	Moderate	Low	Moderate	Low	Low	Moderate

subgroup analysis, sensitivity analysis, and reporting bias. Subsequently, a qualitative synthesis of the results was conducted.

Patients and Public Involvement

The focus of this research was developed following consultations with patients with WAD, however, they were not involved in the analysis of this systematic review.

RESULTS

Literature Search

A total number of 14 studies met the inclusion criteria and were included in the review. The search strategy and reasons for exclusion are outlined in the PRISMA flow chart in Figure 1.

Methodological Quality

The methodological quality of each study is presented in Table 1. Five studies[45–49] were assessed as having a low risk of bias, 4 studies[50–53] as the moderate risk of bias, and 5 studies[54–58] as a high risk of bias. Studies that were assessed as moderate or high risk of bias were mainly due to limitations in the study attrition domain, not adjusting for important confounders, insufficient details for the statistical analysis, and/or poor reporting.

Description of Included Studies

All 14 included studies were cohort studies published between 2001 and 2014. Most of the included studies were conducted in Australia[48,49,51,52,55,59] or Sweden,[46,47,50,56] with only 1 study from other countries including Denmark,[54] UK,[45] Canada[57] Spain,[58] and France[53] (Table 2). A description of the included studies is presented in Table 2, with additional details provided as a Supplementary File S2 (Supplemental Digital Content 2, http://links.lww.com/CJP/A851).

The total number of participants included in the studies was 5954 (14 studies), with a sample size ranging from 76 to 2280 for single studies. Most participants were recruited from emergency departments, while only 1 study included patients referred from an insurance company.[47] The average age of the participants included in the studies ranged from 34 to 37, and the percentage of women ranged between 49% to 71%. The follow-up time ranged from 3 months to 3 years, with most studies investigating the prognostic ability of physical factors on outcomes at 6 and/or 12 months. The reported loss at follow-up ranged from 0%[52] to 18%[58] at 6 months and from 5%[46] to 41%[47] at 12 months, with more information about loss of follow-up reported in a Supplementary File S3 (Supplemental Digital Content 3, http://links.lww.com/CJP/A852).

Outcome Measures

A variety of outcomes were used by the eligible studies including outcomes related to pain-related disability, pain severity, disability and return to work, and quality of life (Table 3).

Pain-related Disability

Pain-related disability was assessed in 7 studies[47–52,55] that were reported for n = 68 (1%) at a 3-month follow-up,[50] n = 76 (1%) at a 6-month follow-up,[52] n = 625 (11%) at a 12-month follow-up,[50,55] n = 1381 (23%) at a 24-month follow-up,[47] and n = 65 (1%) at 2 to 3 years of follow-up.[51] Different measurement tools were used including the NDI,[48,49,51,52] Neck Pain Outcome Score (NPOS) (modified from Low Back Outcome Score),[55] Pain Disability Index (PDI),[50] and Disability Rating Index (DRI).[47] A cutoff score of 30 on the NDI was considered to be a poor outcome. Scores for Pain Disability Index and Neck Pain Outcome Score were treated continuously with higher scores indicating poorer outcome for the former and good outcomes for the latter. The definition of poor outcomes for DRI was defined as scores > 75th centile (DRI = 22) although this was not clearly stated in the study.

Pain Intensity

Neck pain outcome was assessed in 7 studies,[45–47,50,55,58,59] that were reported for n = 68 (1%) at a 3-month follow-up,[50] n = 891 (15%) at a 6-month follow-up,[57,58] n = 1018 (17%) at a 12-month follow-up,[45,46,50,55,57] n = 176 (3%) at an 18-month follow-up,[57] and n = 1507 (25%) at a 24-month follow-up.[47,57] Neck pain was measured using the 0 to 100 mm Visual Analog Scale (VAS),[45–47,50,55,58] or a self-report of severity and frequency of pain in the neck, shoulder, and/or upper back.[57]

The definition of poor outcomes and the cutoff scores for previous scales were defined differently across the included studies. Atherton et al[45] defined persistent neck pain as pain that lasts 1 day or longer which is present at each follow-up period. Gun et al[55] used the VAS to assess neck pain intensity, but it was

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TABLE 2. Description of Included Studies

References	Cohort Number	Country	Setting (Number of Sites)	Time From Collision to Inclusion in Study	No. Participants	Baseline Age, Mean (SD) (y)	Baseline Sex (% Female)	Intervention Details
Kasch et al[54]	1	Denmark	Emergency units (2)	1 wk	141	35.6 (10.7)	52.1	Participants received different interventions postinjury Treatments included a soft cervical collar, physiotherapy, chiropractic treatment, acetylsalicylic acid, NSAID, acetaminophen, opioids, and blockade
Hartling et al[57]	2	Canada	Emergency department	Within the same day up to 48 h	380	37 (NR)	63.5	Received treatments include advice for using heat, use cold, use collar, neck exercise, rest, and medications
Kyhlback et al[50]	3	Sweden	Orthopedic clinic	Within 3 wk	83	35 (NR)	67	NR
Sterner et al[56]	4	Sweden	Hospital emergency room and general practitioners	Within 1 mo	356	34.1 (12.1)	48.9	NR
Gun et al[55]	5	Australia	Public hospital, medical and physiotherapy practices	Within 6 wk	147	35.6 (NR)	67	NR
Sterling et al[52]	6	Australia	Hospital accident and emergency department, primary care practice, advertisement	Within 1 mo	76	36.27 (12.69)	71	Participants were allowed to pursue any form of treatment Several type of treatments and medications were reported including physiotherapy, chiropractic, acupuncture, simple analgesics, NSAIDs, codeine, antidepressants, steroids, and opioids
Atherton et al[45]	7	UK	Emergency department (4)	Median 8 d	765	Median (IQR): 34 (25-44)	56	NR
Berglund et al[47]	8	Sweden	Insurance company	Within a few days	2280	36 (NR)	54	NR
Sterling et al[51]	6	Australia	Hospital accident and emergency department, primary care practice, advertisement	Within 1 mo	76	36.27 (12.69)	71	Participants were allowed to pursue any form of treatment Due to recall bias, treatments received during the 18 mo period was not recorded
Kivioja et al[46]	9	Sweden	Emergency	Within a week	91	NR	54	Received treatments include analgesics medications, physical therapy, and were encouraged to continue with normal activities

(*Continued*)

TABLE 2. (*continued*)

References	Cohort Number	Country	Setting (Number of Sites)	Time From Collision to Inclusion in Study	No. Participants	Baseline Age, Mean (SD) (y)	Baseline Sex (% Female)	Intervention Details
Cobo et al[58]	10	Spain	Emergency unit	Within 1 mo	682	35.6 (13.5)	66.8	The patients were treated according to the established rehabilitation treatment protocol for neck pain after road traffic accident
Sterling et al[48]	11	Australia, Canada, Iceland	Primary care practices, emergency departments, and through general advertisement	< 3 wk duration	286	35.3 (13.08)	62.6	Physiotherapy was the most common form of treatment. Other treatments received included chiropractic, acupuncture, massage, simple analgesics, NSAIDs, opioid-based medication, and adjuvant medications
Ritchie et al[49]	12	Australia	Emergency departments, primary care practices, and via general advertisement	Within 1 mo	262	37.1 (14.2)	NR	NR
Hours et al[53]	13	France	Emergency, secondary, and intensive care units	At time of accident	253	Reported as age groups from 16 to ≥ 55	68	NR

IQR indicates interquartile range; NR, not reported; NSAID, nonsteroidal anti-inflammatory drug.

reversed so that an increase in score represented an improvement. Kyhlback et al[58] assessed pain intensity using the VAS as a continuous outcome where the patients rated the pain experienced at the moment of completing the questionnaire. Besides defining outcomes continuously, other studies categorized the outcomes into good and poor outcomes. Kivioja et al[57] categorized the VAS into 2 groups, with recovered from neck pain as <30 VAS on a 100 mm scale and severe neck pain defined as > 30 VAS, whereas Berglund et al[47] categorized VAS into low (0 to 30), moderate (31 to 54) and severe (55 to 100). Similarly, Cobo et al[58] categorized the VAS into mild (0 to 30), moderate pain (31 to 59), and severe pain (60 to 100). Last, Hartling et al[57] used a self-report questionnaire where poor outcomes were defined as pain in the neck, shoulder, and/or upper back that reached thresholds of intensity and frequency ≥ 3.

Disability and Return to Work

Outcomes related to disability and return to work were assessed in 2 cohorts[54,56] that were assessed at 6- and 12-month follow-ups,[54] and n = 296 (5%) at about a 16-month follow-up.[56] This was measured using self-reported questionnaires that are related to handicap, disability, and work situation. Poor outcomes in these measures were categorized arbitrarily as described in Table 3.

Quality of Life

Quality of life was assessed in one study,[53] at a 12-month follow-up (n = 171; 3%). It was measured using the World Health Organization Quality of Life tool which was dichotomised into the satisfactory or unsatisfactory quality of life and health status.

Prognostic Factors (Narrative Synthesis)

A total of 7 baseline measures of PF were synthesized qualitatively (Table 3).

Neck Pain related Disability

The association between baseline NDI and outcomes (pain intensity and pain-related disability) after a whiplash injury was assessed in 5 studies,[45,48,49,51,52] including a total of 1389 (23%) participants. All studies (3 low, 2 moderate, 1 high risk of bias) indicated that initial high scores of NDI were significantly associated with poor outcomes in patients with acute WAD. This association was also confirmed in multivariate linear and logistic regression analysis where NDI remain associated with poor outcomes following injury.[49,51,52]

Quebec Classification of WAD (Grade I to III)

The association between initial WAD grade II and outcomes was assessed in 7 studies[45 47,50,53,57,58] including a total of 4534 (76%) participants. Five studies (2 low, 2 moderate, 1 high risk of bias) found that initial WAD grade II was not significantly associated with neck pain,[45,46,58] neck pain-related disability,[50] or quality of life[53] following a whiplash injury. However, 3 studies (1 low, 1 moderate, 1 high risk of bias) found that WAD grade II was significantly associated with higher scores of neck pain[47,50] and the presence of long-term symptoms[57] following injury. This

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TABLE 3. Summary of Included Physical Prognostic Factors and Outcomes

References	Cohort Number	Prognostic Factor: Measurement, Instruments, and Definition	Outcome: Measurement, Definition, and Time Point	Length of Follow-up	Analysis	Findings
Kasch et al[54]	1	*Active cervical range of motion:* Neck flexion, extension, left/right lateral flexion, and left/right rotation measured using an inclinometer Dichotomized variable: total ROM of 2 SD below mean in control participants was considered as a risk factor *Neck flexion/extension submaximal (60%) workload:* Product of duration and load of an isometric endurance task for neck flexion/extension Dichotomize variable: workload of 2 SD below mean in control participants was considered as risk factor	*Disability and return to work:* Measurement tool: measured by a questionnaire composed of 6-item ranging from work capacity following injury to receiving pension due to injury Reduced working hours/capacity, missing/changing job, receiving job training, and receiving pension was regarded as handicap	6 and 12 mo	Cox regression analysis	Reduced active cervical ROM increased risk of handicap by a factor of *b* 2.5 ($P < 0.01$) after 1 y, and by a factor of *b* 2.1 after 6 mo Neck muscle workload did not significantly predict long-term handicap at 1 y or 6 mo (*P* 0.39)
Hartling et al[57]	2	*Quebec Classification of WAD (I-III):* Grade II of Quebec Classification was modified by subdividing patients into 2 groups: individuals with point tenderness and normal ROM and individuals with point tenderness and limited ROM	*Pain severity:* Measurement tool: measured by the severity and frequency of pain in the neck, shoulder, and/or upper back Defined operationally as the presence of at least one of neck pain, upper back pain, or shoulder pain that met the predefined thresholds of intensity and frequency (≥ 3), provided by self-report	6, 12, 18, and 24 mo Outcome at 6 mo was considered as the primary outcome	Logistic regression analysis	WAD grade and presence of both tenderness and limited ROM were prognostic factors of presence of long-term symptoms
Kyhlback et al[50]	3	*Quebec Classification of WAD:* Severity of initial injury measured using grade	*Pain-related disability:* Measurement tool: Pain Disability Index Was chosen to measure general and domain-specific disability related to pain (0-70 points) Measured continuously with no dichotomization *Persistent neck pain:* Measurement tool: VAS Was used to assess pain intensity where the patients rated the pain experienced at the moment of survey Measured continuously with no dichotomization	3 and 12 mo	General linear model	WAD grade was not a significant predictor of pain-related disability at 3 or 12 mo WAD grade was a significant predictor of VAS at 12 mo follow-up
Sterner et al[56]	4	*Quebec Classification of WAD:* Severity of initial injury measured using Quebec classification of WAD I, II, III	*Disability and return to work interview:* Disability related to the whiplash trauma Measured using a questionnaire that included items about the perceived effect of	16 ± 2 mo after injury	Univariate and multivariate logistic regression analysis	WAD grades II-III was associated with poor prognosis

(*Continued*)

TABLE 3. (*continued*)

References	Cohort Number	Prognostic Factor: Measurement, Instruments, and Definition	Outcome: Measurement, Definition, and Time Point	Length of Follow-up	Analysis	Findings
			whiplash injury on daily living, leisure activities, and work situation Graded into 4 levels: none or minor; symptoms affecting work or leisure but not sick leave; change of work task; sick leave due to the accident			
Gun et al[55]	5	Physical Component Scale of Short-Form 36 (SF-36) Questionnaire: One subscale of SF-36 that measures the patient's own perception of his/her physical well-being Measured continuously	*Pain-related disability:* Measurement tool: Neck Pain Outcome Score (NPOS): The NPOS was obtained by modifying the Low Back Outcome Score questions by changing the focus of the questions from back pain to neck pain NPOS was structured so that an increase in score represents improvement Measured as a continuous outcome *Persistent neck pain* Measurement tool: VAS Used to assess pain intensity VAS was structured so that an increase in score represents improvement Measured as a continuous outcome	12 mo	Linear and logistic regression	Physical Component Summary of SF-36 was not significantly associated with improvement in VAS after 12 mo follow-up
Sterling et al[52]	6	*Active ROM:* Measured in 3 directions using an electromagnetic, motion-tracking device *Joint position error:* Defined as the participants' ability to relocate the head to natural position following active cervical left and right rotation and extension Measured using an electromagnetic, motion-tracking device *Superficial neck flexor muscle activity:* Surface electromyography was used to measure the activity of the sternocleidomastoid muscles during the craniocervical flexion test (CCFT) *Pain-related disability:* Measured continuously	*Pain-related disability:* Measurement tool: NDI Dichotomised at 6 mo postinjury to: Recovered (NDI < 8) Mild pain and disability (NDI 10-28) Moderate/severe pain and disability (NDI > 30)	6 mo	Linear and logistic regression	*Multivariate regression:* Initial NDI score and left rotation ROM were significant predictors of NDI at 6 mo *Logistic regression:* Initial NDI score was significant predictor to the group with persistent moderate/severe symptoms at 6 mo Initial NDI score and decreased range of cervical extension were significant predictors of membership to the group with persistent mild symptoms versus recovery at 6 mo
Atherton et al[45]	7	*Pain-related disability:* Dichotomize variable: NDI scores were categorized into tertials	*Persistent neck pain:* Measurement tool: measured by VAS which was used to indicate the	12 mo	Poisson regression	High scores of neck disability was significantly associated with persistent neck pain

(*Continued*)

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TABLE 3. (*continued*)

References	Cohort Number	Prognostic Factor: Measurement, Instruments, and Definition	Outcome: Measurement, Definition, and Time Point	Length of Follow-up	Analysis	Findings
		categorization of low, medium, and high *Quebec Classification of WAD:* From collected data, the severity of WAD was judged Severity of initial injury measured using grade Dichotomize variable: categorized into I, II, III classifications *Limitation of neck movement:* Measurement: information was gathered regarding the neck movement using a standard form Dichotomize variable: yes/no	presence of pain in the neck area lasting for 1 d or longer in the week before questionnaire completion Persistent neck pain considered as the presence of pain in the postcollision and at each follow-up point (1, 3, 12 mo)			Grade II (1.2 [0.8-1.8]) and III (1.5 [0.7-3.4]) were not significantly associated with the persistent neck pain) compared with those with grade I injuries Limited ROM was not associated with persistent neck pain 0.9 (0.5-1.6)
Berglund et al[47]	8	*Subjective severity of whiplash injury by Quebec Classification of WAD:* Severity of initial injury measured using Quebec classification of WAD I, II, III	*Persistent neck pain:* Measurement tool: VAS (scale 0-100) VAS was treated a continuous and categorized into 3 groups: Low neck pain (0-30 VAS) Moderate neck pain (31-54 VAS) Severe (55-100) *Pain-related disability:* Measurement tool: DRI The physical disability was assessed using the 12-item Was trichotomized and the cutoffs were the median (DRI 6) and the 75th centile (DRI 22) as measured on the baseline questionnaire	24 mo	Linear and logistic regression	*Self-reported neck pain:* Grade II and III were associated with having a higher neck pain intensity category at follow-up OR 1.5, OR 3.0, respectively *Disability:* A more severe whiplash injury was associated with having a higher degree of disability at follow-up
Sterling et al[51]	6	*ROM:* Measured in the direction of flexion/extension and left/right rotation directions using an electromagnetic, motion-tracking device Left rotation ROM was used in linear regression model, and cervical extension ROM was used in logistic regression model *Joint position error:* Defined as the participants' ability to relocate the head to neutral head position following active cervical left and right rotation and extension	*Pain-related disability:* Measurement tool: NDI Dichotomised at 2-3 y postinjury to: Recovered (NDI < 8) Mild pain-related disability (NDI 10-28) Moderate/severe pain-related disability (NDI > 30)	2-3 y postinjury	Linear and logistic regression	*Linear regression:* Initial NDI scores predict poor NDI scores at 2 y The previously significant prognostic factor left ROM rotation, was not significant predictor at 2-3 y *Logistic regression:* Initial NDI score was significant predictor to the group with persistent moderate/severe symptoms at 2-3 y Initial NDI score was significant predictor of membership to the group with persistent mild symptoms versus recovery at 6 mo

(*Continued*)

TABLE 3. (*continued*)

References	Cohort Number	Prognostic Factor: Measurement, Instruments, and Definition	Outcome: Measurement, Definition, and Time Point	Length of Follow-up	Analysis	Findings
		Measured using an electromagnetic, motion-tracking device *Superficial neck flexor muscle activity:* Surface electromyography was used to measure the activity of the superficial neck muscles during the Craniocervical Flexion Test (CCFT) *Pain-related disability:* Measured continuously				The previously significant prognostic factor, cervical extension ROM, was not significant predictor at 2-3 y
Kivioja et al[46]	9	*Quebec Classification of WAD:* Severity of initial injury measured using Quebec classification of WAD I, II, III	*Persistent neck pain:* Measurement tool: VAS (scale 0-100) Categorized into 2 groups: Severe neck pain (> 30 VAS) Recovered (< 30 VAS)	1 y	Univariate and multivariate logistic regression	The WAD-classification did not predict persistent neck pain
Cobo et al[58]	10	*Quebec Classification of WAD:* General description of the grades were given. The factor was dichotomized into WAD I and WAD II	*Persistent neck pain:* Measurement tool: VAS (scale 0-100) Measured at 6 mo postinjury and categorized into: Mild pain 0-30 Moderate pain 31-59 Severe pain 60-100	6 mo	Linear and multiple linear regression (stepwise method)	WAD grades were not related with poor recovery of VAS 6 mo after whiplash injury
Sterling et al[48]	11	*Pain-related disability:* Measurement tool: NDI used a continuous measure *Active ROM:* Measured using an electromagnetic, motion-tracking device Only left rotation was included in the prediction model as it was a validation study for a previous model	*Pain-related disability:* Measurement tool: NDI Dichotomized at 12 mo postinjury to: Mild or no disability (NDI 0-28) Moderate to severe disability (NDI 30-100)	12 mo	Multivariate regression analysis	*Pain-related disability:* Initial scores of NDI were a significant predictor of poor outcomes 12 mo postinjury *Active ROM:* Neck left ROM was not a significant predictor of poor outcomes in NDI 12 mo postinjury
Ritchie et al[49]	12	*Pain-related disability* Measurement tool: NDI *Active ROM:* Measured using an electromagnetic, motion-tracking device Total neck rotation (sum of left and right neck rotation, flexion and extension) was included in the present study	*Pain-related disability* Measurement tool: NDI Dichotomised at 12 mo postinjury to: Having developed chronic pain-related disability (NDI $\geq 30\%$) Partially/fully recovered (NDI $<30\%$)	12 mo	Univariate and multivariate logistic regression (backward stepwise)	*Univariate:* Increased initial NDI and decreased initial ROM were significantly associated with increased odds of chronic moderate/severe disability vs. recovered/milder disability *Multivariate:* Following a backwards stepwise multiple logistic regression, initial NDI, was significantly associated with moderate to severe disability
Hours et al[53]	13	*Quebec Classification of WAD:* General description of the grades were given. The factor was dichotomised into WAD I and WAD II	*QOL:* Measurement tool: The World Health Organization Quality of Life tool (scale 0-100) QOL was expressed as	12 mo	Linear and multiple Poisson regression	*QOL:* Grade I (OR 1.17; CI: 0.79-1.74) and II (OR 0.84; CI: 0.59-1.18) were not associated with

(*Continued*)

TABLE 3. (*continued*)

References	Cohort Number	Prognostic Factor: Measurement, Instruments, and Definition	Outcome: Measurement, Definition, and Time Point	Length of Follow-up	Analysis	Findings
			dichotomous variables: satisfactory vs. unsatisfactory QOL; and satisfactory vs. unsatisfactory with health status			poor QOL 12 mo postinjury

CI indicates confidence interval; DRI, Disability Rating Index; NDI, Neck Disability Index; OR, odds ratio; QOL, quality of life; ROM, range of motion; VAS, Visual Analog Scale; WAD, whiplash-associated disorder.

narrative analysis showed inconclusive evidence regarding the predictive ability of WAD grade II.

The association between baseline WAD grade III and outcomes was assessed in 3 studies[45 47] including a total of 3136 (60%) participants. With regards to initial WAD III, one study (low risk of bias) found that it was a significant predictor of higher pain scores,[47] while 2 studies (2 low risk of bias) found no significant association with pain intensity after a whiplash injury.[45,46] There was inconclusive evidence about the prognostic ability of WAD grade III.

The predictive ability of WAD grade I and a combination of WAD grades II and III were assessed in 3 studies[53,56,58] including a total of 935 (16%) and 356 (7%) participants, respectively. Cobo et al[58] (high risk of bias) and Hours et al[53] (moderate risk of bias) found that WAD grade I was not a predictor of poor outcome on pain intensity at 6 months and on quality of life at 12 months after the injury. Sterner et al[56] (high risk of bias) found that the combined WAD grades II and III were associated with poor outcomes with regards to disability and return to work.

Neck ROM

The association between baseline neck ROM and outcome was assessed in 6 studies[45,48,49,51,52,54] including a total of 1530 (26%) participants. Kasch and colleagues (high risk of bias) found that reduced total active cervical ROM increased the risk of disability at 6 and 12 months. Decreased neck left rotation and extension at baseline were significantly associated with NDI 6 months following WAD[52] and at 12 months when all neck movements were combined.[49] These factors were no longer predictive of NDI when measured at 12 months,[48] after 2 to 3 years,[51] or when entered into multiple logistic regression.[49] Atherton et al[45] (low risk of bias) found that limited ROM (compared with no limited ROM) was not associated with persistent neck pain at a 12-month follow-up.

JPE

Two studies (1 cohort) with n = 76 (2%) were included in investigating the association between JPS error and NDI at 6 months[52] and 2 to 3 years.[51] Both studies (both moderate risk of bias) found no significant association with poor outcomes at 6 months[51] and 2 to 3 years.[52]

Superficial Neck Flexor Muscle Activity

Two studies (1 cohort; both moderate risk of bias), with n = 76 (2%), found that electromyography (EMG) amplitude of the superficial neck muscles was not a significant predictor of the outcome at 6 months[52] or at 2 to 3 years.[51]

Muscle Strength/Endurance

One study (high risk of bias),[54] including n = 141 (3%) participants, found that the ability of neck flexion/extension submaximal (60%) workload did not significantly predict long-term disability at 6 months or 1 year.

Functional Status

One study (high risk of bias),[55] including n = 147 (2.8%) participants, found that higher scores on the Physical Component Summary measure of the SF-36 was not significantly associated with improvement in neck pain at a 12-month follow-up.[55]

Level of Evidence (GRADE)

A summary of the quality of evidence of each physical factor in this review is presented in Table 4. The quality of evidence was downgraded from ‘moderate’ to ‘very low’ mostly due to issues concerning the high risk of bias of included studies, inconsistency between effects, and potential publication bias.

The GRADE analysis of NDI showed that there was evidence of low quality that baseline NDI was significantly predictive of poor outcome following a whiplash injury. Similarly, very low-quality evidence existed for the predictive ability of combined grade II and III for poor outcomes in patients with WAD. Inconclusive evidence with very low quality was found for the predictive ability of initial neck range of movement, WAD grade II, and WAD grade III following acute whiplash injury. Evidence of very low quality found that factors related to JPE, neck flexor muscle activity, neck flexor muscle strength/endurance, functional status, and WAD grade I were not predictive of poor outcome.

DISCUSSION

This review synthesized the evidence on the prognostic ability of baseline measures of PF in patients with acute WAD, based on 14 cohort studies including a total of 5954 participants. The key findings from this review confirmed that initial higher neck pain-related disability and higher WAD grade are associated with poor outcomes, while there is inconclusive evidence that neck ROM, JPE, activity of the superficial neck muscles, muscle strength/endurance, and perceived functional capacity are not predictive of poor outcome. The level of evidence of most current findings was judged as very low as assessed by GRADE. Finally, this systematic review revealed that there were no primary studies that attempted to investigate the association between more contemporary measures of PF such as the smoothness of neck movement, variability of neck motion,

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TABLE 4. Summary of Findings and Overall Quality as Assessed With GRADE

			GRADE Elements					
Potential Prognostic Factor	No. Participants (% From the Total)	No. Studies (Cohorts)	Risk of Bias	Inconsistency	Indirectness	Imprecision	Publication Bias	Level of Evidence
NDI	1389 (23)	5	✓	✓	✓	✓	×	Low
Grade I	935 (16)	2	×	✓	✓	×	×	Very Low
Grade II	4534 (76)	7	✓	×	✓†	✓	×	Very Low
Grade III	3136 (60)	3	✓	×	✓†	✓	×	Very Low
Grade II and III	356 (7)	1	×	×	NA*	✓	×	Very Low
JPE	76 (2)	2	×	×	✓	✓	×	Very Low
Neck flexor muscle activity	76 (2)	2	×	×	✓	✓	×	Very Low
Neck flexor muscle strength/endurance	141 (3)	1	×	×	NA*	✓	×	Very Low
Functional status	147 (3)	1	×	×	NA*	✓	×	Very Low
Neck ROM	1530 (26)	6	✓	×	×‡	✓	×	Very Low

For GRADE elements: ✓, no serious limitations; ×, serious limitations.
For overall quality of evidence: High (++++), moderate (+++), low (++), very low (+).
*Only one study.
†Whiplash-associated disorder grade collected from self-report and some from objective measures.
‡Different methods for measuring neck ROM.
CI indicates confidence interval; GRADE, Grading of Recommendations Assessment, Development and Evaluation; JPE, joint position error; NA, not applicable; NDI, Neck Disability Index; ROM, range of motion.

and coactivation of neck muscles with outcome following a whiplash injury.

Pain related Disability

This review found that initial higher scores of pain-related disability measured by the NDI was a prognostic factor of poor outcome following a whiplash injury. This finding is consistent with previous reviews that reported that initial greater pain-related disability predicted poor outcome following whiplash injury.[5,10,21,28] Although the findings were consistent between reviews, the findings should be interpreted with caution due to the heterogeneity of the used outcomes and the wide variability in the cutoff values, as reported previously.[60] Moreover, our review found the level of evidence of such association to be low, which means we have very little confidence in the estimate of such association.

Quebec Classification of WAD (Grade I to III)

Being graded with neck pain but with no physical signs (WAD grade I) following a whiplash injury did not show any predictive ability of poor outcome when compared with those with no reports about neck pain (grade 0).[58] One drawback for WAD grade I is that it does not measure the intensity of neck pain. Therefore, using grade I solely for its prognostic ability may not provide useful clinical information.

Five studies found that WAD grade II (neck pain with physical signs) was not associated with poor outcome following whiplash injury[45,46,50,53,58] while 3 studies[47,50,57] found a significant association.

Inconclusive evidence was observed for WAD grade III compared with those with grade II. One study found that having neurological symptoms in addition to neck pain and physical signs was a significant predictor of higher neck pain scores,[47] while 2 studies found no significant association with neck pain after whiplash injury.[45,46] Even though the estimated effects of these 2 studies were not significant,[45,46] the direction of estimation was in favor with an association of poor outcome. This was evident when these 3 studies were included in a meta-analysis by Walton et al[21] who showed WAD grade III to be significantly associated with persistent neck pain 12 months postinjury. Moreover, the prognostic ability of WAD III was also confirmed in a recent systematic review.[31] It could be inferred that, although we found inconsistency in the association between WAD grade III and poor outcomes, patients with physical and neurological symptoms postinjury may develop persistent poor outcomes more so than those with no neurological deficits.

Neck ROM

Our review found inconclusive evidence about whether reduced cervical motion is associated with poor outcome following a whiplash injury. This finding is in line with previous reviews that found a limited association between restricted neck motion and persistent disability,[23,28,29] whereas no such association was found in another review.[10] One explanation for the different findings could be attributed to the different approaches used to measure and dichotomize neck motion by the included studies. For example, Kasch et al[54] defined neck restriction as total ROM <2 SD below mean in control participants, Atherton et al[45] defined restricted neck motion as yes/no based on the patients' own perception, whereas studies by Sterling and colleagues,[51,52] measured neck motion in each direction.

JPE and Activity of the Superficial Neck Muscles

Our review found that neck proprioception measured as JPE, EMG amplitude of the superficial neck flexor muscles during craniocervical flexion, and workload in the neck flexors and extensors were not associated with poor outcome in patients with WAD. This is consistent with the findings that were reported from a previous review.[23] However, the previous findings were based on just 1 cohort for JPE and EMG[51,52] and 1 for muscle strength/endurance.[54] It is evident that further studies are needed to investigate the predictive ability of changes in muscle behavior and proprioception in patients following a whiplash injury.

Functional Status

The SF-36 consists of different subscales of functional status including subscales related to Physical Functioning, Role Physical, Bodily Pain, General Health, Vitality, Social Functioning, Role Emotional, and Mental Health.[37] These subscales are combined into 2 scales named the Physical Component Summary Score and Mental Component Summary Score.[37] Our review found that Physical Component Summary of SF-36 was not significantly associated with a reduction of neck pain intensity at a 12-month follow-up. The Physical Component Summary of SF-36 was not reported in previous reviews but rather a complete overall score,[5] Bodily Pain score,[28] or Role Emotional score,[28] which found to be associated with poor outcomes following a whiplash injury. Given the limited evidence about the association between self-reported perceived physical functioning and outcomes in WAD, further studies are required.

Strengths and Limitations

The current review has several strengths. First, the methodology of the current review, including the literature search, was thorough and rigorous and adhered to a published protocol. This review included 13 distinct cohorts compared with only 3 cohorts in the review by Daenen et al[23] that had a similar aim to the current review. In addition, the current study utilized GRADE to assess the overall level of evidence, unlike the earlier study by Daenen et al[23] which did not assess the level of evidence. Further, the list of excluded studies, with their reasons, are available for other researchers to use for future planning of a systematic review (Supplementary File S4, Supplemental Digital Content 4, http://links.lww.com/CJP/A853). Finally, the QUIPS risk of bias tool was tailored specifically for this review and is provided as a Supplementary File S1 (Supplemental Digital Content 1, http://links.lww.com/CJP/A850).

However, there are some limitations that should be noted. Despite our comprehensive search strategy, potential relevant prognostic studies might be possibly missed due to poor reporting and/or if they were published in a language other than English. Furthermore, the initial agreement on the risk of bias ratings and criteria in this review varied between reviewers, an issue which was pointed out previously.[61] However, this risk was minimized by conducting multiple discussion sessions among the reviewers which resulted in tailoring the QUIPS criteria to this review; this has been provided as a Supplementary File for Transparency S1 (Supplemental Digital Content 1, http://links.lww.com/CJP/A850). The calculation of agreement between assessors in the risk of bias and GRADE evaluation was not planned *priori* for this review and therefore was not conducted.

CONCLUSIONS

This review provided evidence, which overall was of low to very low quality, that higher pain-related disability and higher WAD grade are associated with poor outcome following a whiplash injury. There was inconclusive evidence about the prognostic ability of factors such as the range of neck movement, JPE, the activity of the superficial neck muscles, muscle strength/endurance, and perceived functional status. More contemporary measures of physical function such as neck movement velocity, smoothness of movement, and coactivation of neck muscles have not been investigated, and therefore further research in this area is required.

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Appendix 8: STROBE Statement-Checklist of items that should be included in reports of case-control studies

	Item No	Recommendation	Page No
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	1
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	1
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	4-5
Objectives	3	State specific objectives, including any prespecified hypotheses	5
Methods			
Study design	4	Present key elements of study design early in the paper	5
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	5-7
Participants	6	(*a*) Give the eligibility criteria, and the sources and methods of case ascertainment and control selection. Give the rationale for the choice of cases and controls	6
		(*b*) For matched studies, give matching criteria and the number of controls per case	NA
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	8-10
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	8-10
Bias	9	Describe any efforts to address potential sources of bias	NA
Study size	10	Explain how the study size was arrived at	10
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	10
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	10
		(*b*) Describe any methods used to examine subgroups and interactions	NA
		(*c*) Explain how missing data were addressed	NA
		(*d*) If applicable, explain how matching of cases and controls was addressed	NA
		(*e*) Describe any sensitivity analyses	NA
Results			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	11
		(b) Give reasons for non-participation at each stage	NA
		(c) Consider use of a flow diagram	NA
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	11-12
		(b) Indicate number of participants with missing data for each variable of interest	NA
Outcome data	15*	Report numbers in each exposure category, or summary measures of exposure	NA
Main results	16	(a) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	NA
		(b) Report category boundaries when continuous variables were categorized	NA
		(c) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	NA
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	NA

Discussion			
Key results	18	Summarise key results with reference to study objectives	13
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	15
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	13-15
Generalisability	21	Discuss the generalisability (external validity) of the study results	15
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	22

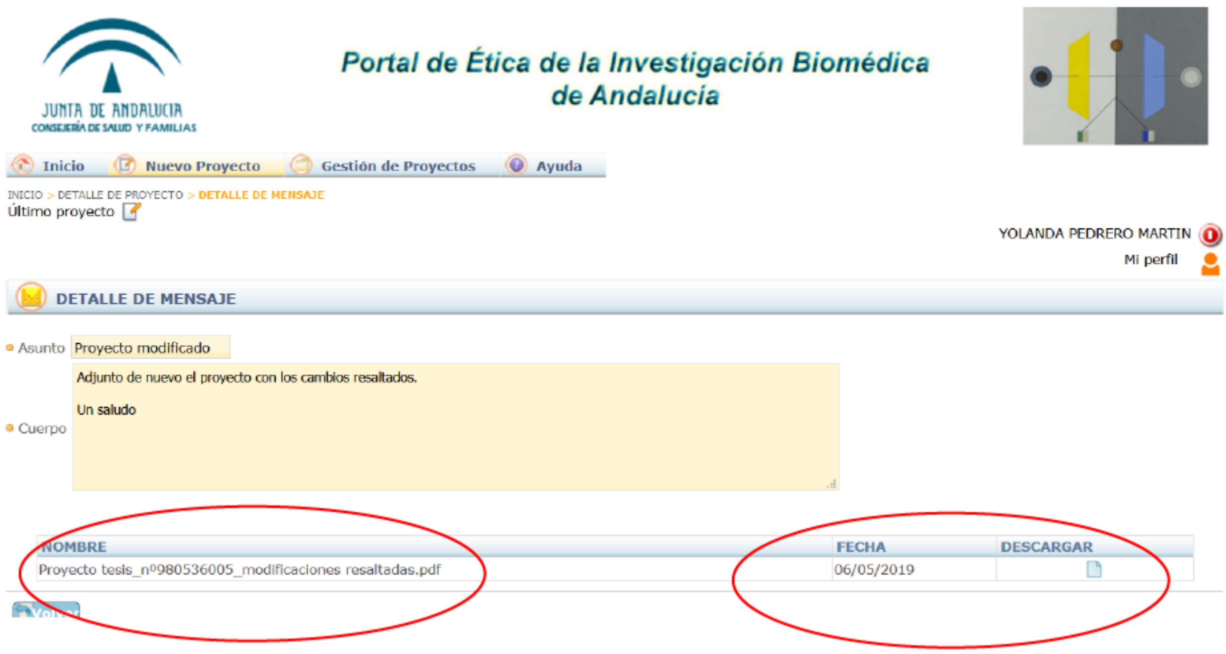
*Give information separately for cases and controls.

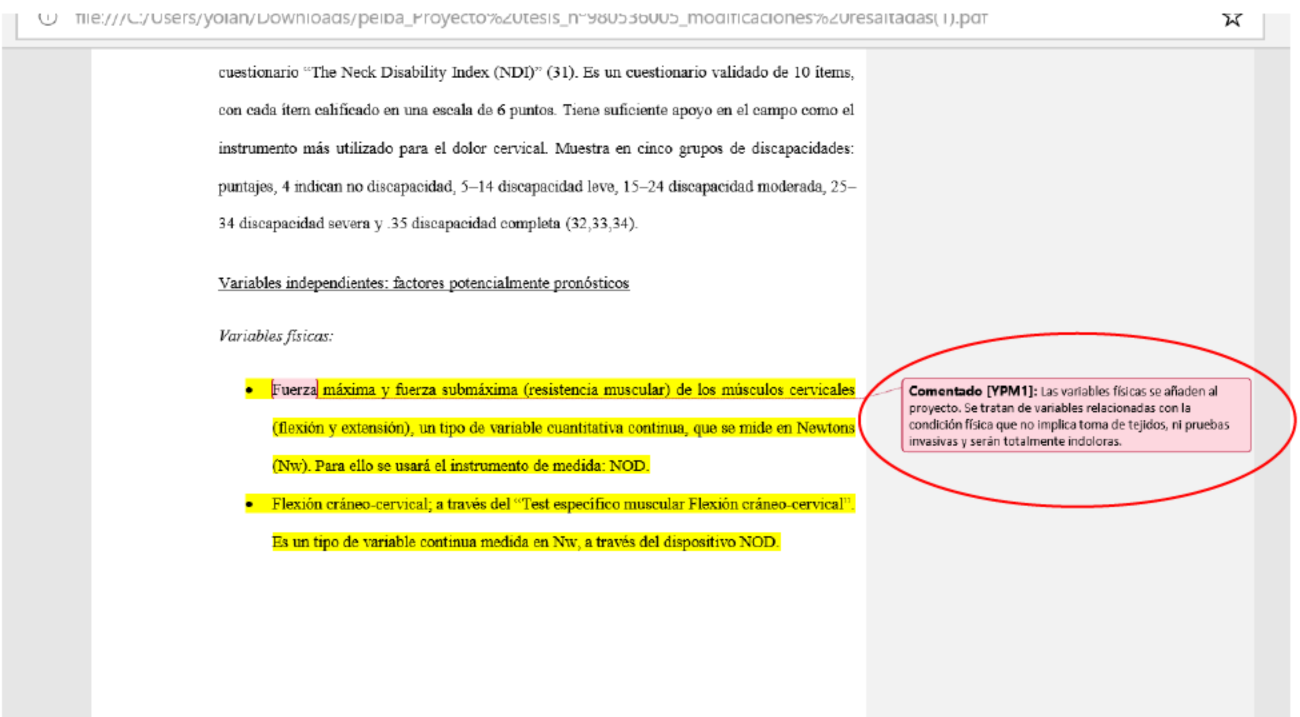
Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at http://www.strobe-statement.org.

Appendix 9: Amendments to ethical application to incorporate physical measures in people with acute WAD

EXTENSION FOR THE ETHICS APPROVAL

On April 14th, 2019, we applied for some changes in the Ethics Committee (Portal de la Etica de la Investigacion Biomedica de Andalucia). These changes consisted of the inclusion of all the variables included in this thesis as an extension of a previous ethical approval granted for a similar project (psychological factors and whiplash disorders). On May 4th, 2019, the Ethical Committee accepted all the changes and released the new approval (**Appendix 10**).




file:///C:/Users/yolan/Downloads/peiba_Proyecto%20tesis_n°980536005_modificaciones%20resaltadas(1).pdf

cuestionario "The Neck Disability Index (NDI)" (31). Es un cuestionario validado de 10 ítems, con cada ítem calificado en una escala de 6 puntos. Tiene suficiente apoyo en el campo como el instrumento más utilizado para el dolor cervical. Muestra en cinco grupos de discapacidades: puntajes, 4 indican no discapacidad, 5–14 discapacidad leve, 15–24 discapacidad moderada, 25–34 discapacidad severa y .35 discapacidad completa (32,33,34).

Variables independientes: factores potencialmente pronósticos

Variables físicas:

- Fuerza máxima y fuerza submáxima (resistencia muscular) de los músculos cervicales (flexión y extensión), un tipo de variable cuantitativa continua, que se mide en Newtons (Nw). Para ello se usará el instrumento de medida: NOD.
- Flexión cráneo-cervical; a través del "Test especifico muscular Flexión cráneo-cervical". Es un tipo de variable continua medida en Nw, a través del dispositivo NOD.

Comentado [YPM1]: Las variables físicas se añaden al proyecto. Se tratan de variables relacionadas con la condición física que no implica toma de tejidos, ni pruebas invasivas y serán totalmente indoloras.

Appendix 10: Ethical approval (in Spanish)

Comité de Ética de la Investigación Provincial de Málaga

Servicio Andaluz de Salud
CONSEJERÍA DE SALUD

Dra. Dña. Gloria Luque Fernández, Secretaria del CEI Provincial de Málaga

CERTICA:

Que en la sesión de CEI de fecha: 30/05/2019 ha evaluado laMS de la propuesta de MS de D/Dña.: Yolanda Pedrero Martín, referido al Proyecto de Investigación: "Influencia de los factores psicológicos en la cronicidad del latigazo cervical. Estudio longitudinal prospectivo
".

Este Comité lo considera ética y metodológicamente correcto.

La composición del CEI en esta sesión es la siguiente:

Dra. Ana Alonso Torres (UGC Neurociencias)
Dra. Encarncación Blanco Reina (Farmacología Clínica)
Dr. José C. Fernández García (UGC Endocrinología y Nutrición)
Dra. Marta Camacho Caro (UGC Ginecología)
Dra. Paloma Campo Mozo (UGC Alegia)
Dr. Antonio E. Guzmán Guzmán (UGC Farmacia Hospitalaria)
Dra. Mª Victoria de la Torre Prados (UGC UMI)
Dña. Carmen López Gálvez del Postigo (Miembro Lego)
Dr. Antonio López Téllez (Médico de Familia)
Dr. José L. Guerrero Orriach (UGC Anestesia y Reanimación)
Dra. Gloria Luque Fernández (Investigación)
Dra. Mª Mercedes Márquez Castilla (Médico Familia)
Dra. Cristobalina Mayorga Mayorga (Laboratorio)
Dra. Eva Mingot Castellanos (UGC Hematología)
D. Ramón Porras Sánchez (RRHH-Abogado)
Dr. Manuel Herrera Gutiérrez (UGC UCI)
Dr. Rafael Carvia Ponsaille (Anatomía Patológica)
Dra. Mª Carmen Vela Márquez (Farmacéutica Distrito)
Dra. Leonor Ruíz Sicilia (UGC Salud Mental)

Lo que firmo en Málaga, a 4 de mayo de 2019

Fdo.: Dra. Gloria Luque Fernández
Secretaria del CEI

Appendix 11: Participant information sheet for people with acute neck pain (in Spanish)

UNIVERSIDAD DE MÁLAGA

Vital&Clinic
AL SERVICIO DE TU SALUD

¿Las medidas físicas mejoran la predicción del dolor y la discapacidad tras un latigazo cervical?

Nos gustaría invitarle a participar en nuestro estudio de investigación…

Antes de decidir participar, es importante saber por qué se realiza la investigación y qué implicará. Tómese el tiempo de leer atentamente la siguiente hoja de información.

¿Cuál es el objetivo del estudio?

Este estudio tiene como objetivo comprender por qué algunas personas después de un latigazo cervical se recuperan temprano, mientras que otras continúan experimentando dolor. Las personas a menudo mejorarán en unas pocas semanas o meses, pero para algunas personas puede durar más y limitar severamente sus actividades. Estamos interesados en comprender por qué los síntomas de algunas personas duran más que otras. Su participación en esta investigación es importante ya que podría ayudarnos a identificar las características relacionadas con la recuperación que nos ayudan a desarrollar nuevos enfoques para la evaluación y tratamiento de personas con latigazo cervical.

¿Puedo participar?

Puedes participar en este estudio si:

- Tienes 16 años o mayor.
- Estuvo en un accidente automovilístico o lesión deportiva en los 15 días anteriores
- Síntomas experimentados como dolor de cuello, dolor de cabeza o síntomas en el brazo.

No puedes participar en este estudio si:

- Tuvo fracturas o luxaciones en el cuello debido al accidente
- Pérdida de conciencia o memoria debido al accidente
- Cirugía previa de cuello
- Otros síntomas como heridas abiertas, trastornos espinalesmalignos, trastornos mentales, abuso de fármacos o alcohol, uso regular de analgésicos.

UNIVERSIDAD DE MÁLAGA

Vital&Clinic
AL SERVICIO DE TU SALUD

¿Qué ocurrirá si participas en el estudio?

Una vez que haya aceptado participar, le pediremos que asista a una sesión en nuestro centro privado de fisioterapia. Puede retirarse del estudio en cualquier momento sin dar ninguna razón. Si elige retirarse del estudio, su atención médica no se verá afectada de ninguna manera.

En la clínica,

Completará algunos cuestionarios.

Realice algunos movimientos del cuello, como girar la cabeza y mover la cabeza hacia arriba y hacia abajo, para medir el movimiento del cuello.

Realice el movimiento anterior, pero con los ojos cerrados.

Realice 2 contracciones máximas de tres movimientos (figura 1) para probar la fuerza de los músculos del cuello en la parte delantera y trasera del cuello. Seguido de contracciones mínimas (20% de su fuerza muscular máxima del cuello) durante 10 segundos para evaluar su capacidad de mantener estas contracciones de manera constante. Durante ambas actividades, se colocarán pequeños electrodos adhesivos sobre los músculos del cuello para registrar la activación muscular.

Figura 1. Asintiendo   Asentir hacia delante   Asentir hacia atrás

Después de 3,6 y 12 meses…

Completa un cuestionario aerca del dolor de cuello.

¿Cuánto tiempo tendré que pasar en total?

La sesión en la clínica durará alrededor de 1,5 horas.

¿Hay algún beneficio para mí si participo?

No hay ningún beneficio específico para usted al participar en este estudio. Sin embargo, esta investigación podría ayudarnos a identificar quién es probable que desarrolle dolor continuo después de una lesión por latigazo cervical, lo que podría llevar a desarrollar nuevos enfoques de evaluación y tratamiento para reducir el riesgo de desarrollar síntomas continuos.

¿Hay algún riesgo para mí si participo?

Los riesgos son bajos, ya que todos los procedimientos son realizados por profesionales experimentados y usted será examinado minuciosamente para asegurarse de que sea seguro participar. Todas las pruebas realizadas no son invasivas. Puede detener el experimento y, si lo desea, puede retirarse del estudio en cualquier momento. Puede experimentar una leve molestia mientras realiza las 2 contracciones máximas. Se proporcionará un tiempo de descanso adecuado a lo largo de las mediciones y se darán períodos de descanso adicionales si es necesario.

¿Mis datos se mantendrán confidenciales?

Toda la información recopilada sobre usted se mantendrá estrictamente confidencial. El formulario de consentimiento que contiene su identificación asignada nunca estará presente en forma electrónica, y se almacenará de forma segura en CPR Spine y solo estará disponible para los investigadores. Todos los datos se almacenarán durante 10 años gestionados de acuerdo con el Reglamento general de protección de datos de la UE 2018.

¿Qué pasará con los resultados del estudio?

Todos los datos para la presentación serán anónimos, lo que significa que su identidad no será revelada de ninguna manera. Los resultados de este estudio se presentarán o compartirán con otros investigadores en forma de presentaciones y documentos científicos, según corresponda.

Si quiere conocer los resultados del estudio, el email para contactar con los investigadores del estudio es: [redacted]

¡Gracias por tomarse el tiempo de leer esto y considerar participar en el estudio!

Appendix 12: Consent form (in Spanish)

Consentimiento Informado

Número Identificación Participante:

Vital&Clinic
AL SERVICIO DE TU SALUD

UNIVERSIDAD DE MÁLAGA

UNIVERSITY OF BIRMINGHAM

¿Las medidas físicas mejoran la predicción del dolor y la discapacidad tras un latigazo cervical?

Caja In c a

1. He ten do a oportun dad de cons derar a nformac ón, hacer preguntas, y han s do respond das sat sfactor amente. ☐

2. Ent endo que m part c pac ón es vo untar a y que soy bre d ret rarme en cua qu er momento, s n dar a guna razón. ☐

3. Acepto que m nformac ón pud era ser usada en nvest gac ón y presentada/pub cada anón mamente en a teratura c entíf ca. ☐

4. Soy cons cente de que m s datos persona es serán procesados para os propós tos descr tos arr ba, de acuerdo a a ey de protecc ón de datos (1998) y a regu ac ón de protecc ón genera de datos (2018). ☐

5. Estoy de acuerdo en part c par en e presente estud o. ☐

Nombre de Part c pante: ....

Fecha: ....

F rma ....

Ema : ....

Número Te éfono: ....

Nombre Invest gador: ....

Fecha: ....

F rma: ....

S qu ere conocer os resu tados de estud o, e ema para contactar con os nvest gadores de estud o es:

Appendix 13: Neck Disability Index (in Spanish)

ANEXO 1

Índice de Discapacidad Cervical

Nombre:
Fecha:
Domicilio:
Profesión:
Edad:

Por favor, lea atentamente las instrucciones:

Este cuestionario se ha diseñado para dar información a su médico sobre cómo le afecta a su vida diaria el dolor de cuello. Por favor, rellene todas las preguntas posibles y marque en cada una SÓLO LA RESPUESTA QUE MÁS SE APROXIME A SU CASO. Aunque en alguna pregunta se pueda aplicar a su caso más de una respuesta, marque sólo la que represente mejor su problema.

Pregunta I: Intensidad del dolor de cuello

- ☐ No tengo dolor en este momento
- ☐ El dolor es muy leve en este momento
- ☐ El dolor es moderado en este momento
- ☐ El dolor es fuerte en este momento
- ☐ El dolor es muy fuerte en este momento
- ☐ En este momento el dolor es el peor que uno se puede imaginar

Pregunta II: Cuidados personales (lavarse, vestirse, etc.)

- ☐ Puedo cuidarme con normalidad sin que me aumente el dolor
- ☐ Puedo cuidarme con normalidad, pero esto me aumenta el dolor
- ☐ Cuidarme me duele de forma que tengo que hacerlo despacio y con cuidado
- ☐ Aunque necesito alguna ayuda, me las arreglo para casi todos mis cuidados
- ☐ Todos los días necesito ayuda para la mayor parte de mis cuidados
- ☐ No puedo vestirme, me lavo con dificultad y me quedo en la cama

Pregunta III: Levantar pesos

- ☐ Puedo levantar objetos pesados sin aumento del dolor
- ☐ Puedo levantar objetos pesados, pero me aumenta el dolor
- ☐ El dolor me impide levantar objetos pesados del suelo, pero lo puedo hacer si están colocados en un sitio fácil como, por ejemplo, en una mesa
- ☐ El dolor me impide levantar objetos pesados del suelo, pero puedo levantar objetos medianos o ligeros si están colocados en un sitio fácil
- ☐ Sólo puedo levantar objetos muy ligeros
- ☐ No puedo levantar ni llevar ningún tipo de peso

Pregunta IV: Lectura

- ☐ Puedo leer todo lo que quiera sin que me duela el cuello
- ☐ Puedo leer todo lo que quiera con un dolor leve en el cuello
- ☐ Puedo leer todo lo que quiera con un dolor moderado en el cuello
- ☐ No puedo leer todo lo que quiero debido a un dolor moderado en el cuello
- ☐ Apenas puedo leer por el gran dolor que me produce en el cuello
- ☐ No puedo leer nada en absoluto

Pregunta V: Dolor de cabeza

- ☐ No tengo ningún dolor de cabeza
- ☐ A veces tengo un pequeño dolor de cabeza
- ☐ A veces tengo un dolor moderado de cabeza
- ☐ Con frecuencia tengo un dolor moderado de cabeza
- ☐ Con frecuencia tengo un dolor fuerte de cabeza
- ☐ Tengo dolor de cabeza casi continuo

Pregunta VI: Concentrarse en algo

- ☐ Me concentro totalmente en algo cuando quiero sin dificultad
- ☐ Me concentro totalmente en algo cuando quiero con alguna dificultad
- ☐ Tengo alguna dificultad para concentrarme cuando quiero
- ☐ Tengo bastante dificultad para concentrarme cuando quiero
- ☐ Tengo mucha dificultad para concentrarme cuando quiero
- ☐ No puedo concentrarme nunca

Pregunta VII: Trabajo y actividades habituales

*Pregunta VII: Trabajo**

- ☐ Puedo trabajar todo lo que quiero
- ☐ Puedo hacer mi trabajo habitual, pero no más
- ☐ Puedo hacer casi todo mi trabajo habitual, pero no más
- ☐ No puedo hacer mi trabajo habitual
- ☐ A duras penas puedo hacer algún tipo de trabajo
- ☐ No puedo trabajar en nada

Pregunta VIII: Conducción de vehículos

- ☐ Puedo conducir sin dolor de cuello
- ☐ Puedo conducir todo lo que quiero, pero con un ligero dolor de cuello
- ☐ Puedo conducir todo lo que quiero, pero con un moderado dolor de cuello
- ☐ No puedo conducir todo lo que quiero debido al dolor de cuello
- ☐ Apenas puedo conducir debido al intenso dolor de cuello
- ☐ No puedo conducir nada por el dolor de cuello

Pregunta IX: Sueño

- ☐ No tengo ningún problema para dormir
- ☐ El dolor de cuello me hace perder menos de 1 hora de sueño cada noche
  Pierdo menos de 1 hora de sueño cada noche por el dolor de cuello*
- ☐ El dolor de cuello me hace perder de 1 a 2 horas de sueño cada noche
  Pierdo de 1 a 2 horas de sueño cada noche por el dolor de cuello*
- ☐ El dolor de cuello me hace perder de 2 a 3 horas de sueño cada noche
  Pierdo de 2 a 3 horas de sueño cada noche por el dolor de cuello*
- ☐ El dolor de cuello me hace perder de 3 a 5 horas de sueño cada noche
  Pierdo de 3 a 5 horas de sueño cada noche por el dolor de cuello*
- ☐ El dolor de cuello me hace perder de 5 a 7 horas de sueño cada noche
  Pierdo de 5 a 7 horas de sueño cada noche por el dolor de cuello*

Pregunta X: Actividades de ocio

- ☐ Puedo hacer todas mis actividades de ocio sin dolor de cuello
- ☐ Puedo hacer todas mis actividades de ocio con algún dolor de cuello
- ☐ No puedo hacer algunas de mis actividades de ocio por el dolor de cuello
- ☐ Sólo puedo hacer unas pocas actividades de ocio por el dolor del cuello
- ☐ Apenas puedo hacer las cosas que me gustan debido al dolor del cuello
- ☐ No puedo realizar ninguna actividad de ocio

*Texto utilizado previamente a los cambios propuestos a raíz de los problemas de comprensión.

Appendix 14: Pain catastrophising scale (in Spanish)

PAIN CATASTROPHIZING SCALE

Todas las personas experimentamos situaciones de dolor en algún momento de nuestra vida. Las personas estamos a menudo expuestas a situaciones que pueden causar dolor como las enfermedades, las heridas, los tratamientos dentales o las intervenciones quirúrgicas.
Estamos interesados en conocer el tipo de pensamientos y sentimientos que usted tiene cuando siente dolor. A continuación se presenta una lista de 13 frases que describen diferentes pensamientos y sentimientos que pueden estar asociados al dolor. Utilizando la siguiente escala, por favor, indique el grado en que usted tiene esos pensamientos y sentimientos cuando siente dolor.

Cuando siento dolor…

1. Estoy preocupado todo el tiempo pensando en si el dolor desaparecerá
    - 0: Nada en absoluto
    - 1: Un poco
    - 2: Moderadamente
    - 3: Mucho
    - 4: Todo el tiempo

2. Siento que ya no puedo más
    - 0: Nada en absoluto
    - 1: Un poco
    - 2: Moderadamente
    - 3: Mucho
    - 4: Todo el tiempo

3. Es terrible y pienso que esto nunca va a mejorar
    - 0: Nada en absoluto
    - 1: Un poco
    - 2: Moderadamente
    - 3: Mucho
    - 4: Todo el tiempo

4. Es horrible y siento que esto es más fuerte que yo
    - 0: Nada en absoluto
    - 1: Un poco
    - 2: Moderadamente
    - 3: Mucho
    - 4: Todo el tiempo

5. Siento que no puedo soportarlo más
    - 0: Nada en absoluto
    - 1: Un poco
    - 2: Moderadamente
    - 3: Mucho
    - 4: Todo el tiempo

6. Temo que el dolor empeore

0: Nada en absoluto
1: Un poco
2: Moderadamente
3: Mucho
4: Todo el tiempo

7. No dejo de pensar en otras situaciones en las que experimento dolor
   0: Nada en absoluto
   1: Un poco
   2: Moderadamente
   3: Mucho
   4: Todo el tiempo

8. Deseo desesperadamente que desaparezca el dolor
   0: Nada en absoluto
   1: Un poco
   2: Moderadamente
   3: Mucho
   4: Todo el tiempo

9. No puedo apartar el dolor de mi mente
   0: Nada en absoluto
   1: Un poco
   2: Moderadamente
   3: Mucho
   4: Todo el tiempo

10. No dejo de pensar en lo mucho que me duele
   0: Nada en absoluto
   1: Un poco
   2: Moderadamente
   3: Mucho
   4: Todo el tiempo

11. No dejo de pensar en lo mucho que deseo que desaparezca el dolor
   0: Nada en absoluto
   1: Un poco
   2: Moderadamente
   3: Mucho
   4: Todo el tiempo

12. No hay nada que pueda hacer para aliviar la intensidad del dolor
   0: Nada en absoluto
   1: Un poco
   2: Moderadamente
   3: Mucho
   4: Todo el tiempo

13. Me pregunto si me puede pasar algo grave
   0: Nada en absoluto
   1: Un poco
   2: Moderadamente
   3: Mucho
   4: Todo el tiempo

Appendix 15: Tampa Scale of Kinesiophobia (in Spanish)

CUESTIONARIO TSK-11SV

Tampa Scale for Kinesiophobia (Spanish adaptation. Gómez-Pérez, López-Martínez y Ruiz-Párraga, 2011)

INSTRUCCIONES: a continuación se enumeran una serie de afirmaciones. Lo que Ud. ha de hacer es indicar hasta qué punto eso ocurre en su caso según la siguiente escala:

1	2	3	4
Totalmente en desacuerdo			**Totalmente de acuerdo**

1. Tengo miedo de lesionarme si hago ejercicio físico.	1	2	3	4
2. Si me dejara vencer por el dolor, el dolor aumentaría.	1	2	3	4
3. Mi cuerpo me está diciendo que tengo algo serio.	1	2	3	4
4. Tener dolor siempre quiere decir que en el cuerpo hay una lesión.	1	2	3	4
5. Tengo miedo a lesionarme sin querer.	1	2	3	4
6. Lo más seguro para evitar que aumente el dolor es tener cuidado y no hacer movimientos innecesarios.	1	2	3	4
7. No me dolería tanto si no tuviese algo serio en mi cuerpo.	1	2	3	4
8. El dolor me dice cuándo debo parar la actividad para no lesionarme.	1	2	3	4
9. No es seguro para una persona con mi enfermedad hacer actividades físicas.	1	2	3	4
10. No puedo hacer todo lo que la gente normal hace porque me podría lesionar con facilidad.	1	2	3	4
11. Nadie debería hacer actividades físicas cuando tiene dolor.	1	2	3	4

Appendix 16: The Quality In Prognostic Studies (QUIPS) tool

Biases	Issues to consider for judging overall rating of 'Risk of bias'	Study Methods & Comments	Rating of reporting	Rating of 'Risk of bias'
Instruct ons to assess the r sk of each potent a b as:	These ssues w gu de your th nk ng and judgment about the overa r sk of b as w th n each of the 6 doma ns. Some ' ssues' may not be re evant to the spec f c study or the rev ew research quest on. These ssues are taken together to nform the overa judgment of potent a b as for each of the 6 doma ns.	Prov de comments or text exerpts n the wh te boxes be ow, as necessary, to fac tate the consensus process that w fo ow.	C ck on each of the b ue ce s and choose from the drop down menu to rate the adequacy of report ng as yes, part a , no or unsure.	C ck on the green ce s; choose from the drop down menu to rate potent a r sk of b as for each of the 6 doma ns as H gh, Moderate, or Low cons der ng a re evant ssues
1. Study Participation	**Goal: To judge the risk of selection bias (likelihood that relationship between *PF* and *outcome* is different for participants and eligible non-participants). IF YES, the information bellow should be reported**			
Method used to identify population	The recru tment of part c pants s descr bed nc ud ng the se ect on process of part c pants and not just the overa number of nc uded part c pants.			
Recruitment period	Per od of recru tment (beg nn ng and end of recru tment) s adequate y descr bed			
Place of recruitment	P ace of recru tment (sett ng and geograph c ocat on) are adequate y descr bed			
Inclusion and exclusion criteria	Inc us on and exc us on cr ter a are adequate y descr bed and n agreement w th those of th s rev ew.			
Adequate study participation?	There s adequate (>67%) part c pat on n the study by e g b e nd v dua s (1).			
Baseline characteristics	The base ne study samp e (.e., nd v dua s enter ng the study) s adequate y descr bed for (T me from njury/trauma to data co ect on, mean age, fema e gender)			
Summary Study participation	**The study sample represents the population of interest on key characteristics, sufficient to limit potential bias of the observed relationship between PF and outcome.**			
2. Study Attrition	**Goal: To judge the risk of attrition bias (likelihood that relationship between *PF and outcome* are different for completing and non-completing participants). For a Yes**			
Proportion of baseline sample available for analysis	Response rate s adequate (67%) (1).			
Attempts to collect information on participants who dropped out	Attempts to co ect nformat on on part c pants who dropped out of the study are descr bed.			
Reasons and potential impact of subjects lost to follow up	Reasons for oss to fo ow up are prov ded.			
Adequate description for participants lost to follow up	There s nformat on ava ab e for those who dropped outs on age, gender, sever ty of wh p ash us ng e ther NDI or WAD grade or any other wh p ash re ated nformat on.			

There are no important differences between participants who completed the study and those who did not	There are no s gn f cant mportant d fferences between part c pants who comp eted the study and those who d d not n regard to age, gender, NDI scores and pa n scores.			
Study Attrition Summary	**Loss to follow-up (from baseline sample to study population analysed) is not associated with key characteristics (i.e., the study data adequately represent the sample) sufficient to limit potential bias to the observed relationship between PF and outcome.**			
3. Prognostic Factor Measurement	**Goal: To judge the risk of measurement bias related to how PF was measured (differential measurement of PF related to the level of outcome). For a Yes there should be**			
A clear definition or description of 'PF' is provided	There shou d be a c ear def n t on of the PF, e.g. how the data was co ected, how the var ab e was measured.			
Method of PF measurement is adequately valid and reliable	There shou d be a reference to a re ab ty/va d ty study or nformat on on these features n the paper and th s paper shou d cover the f e d of nterest (Wh p ash). In the f e d of rehab tat on of chron c pa n we suggest that when d fferent prognost c factors are nc uded w th d fferent RoB, th s ssue shou d be noted and so ved n the synthes s phase of the SR/MA (e.g. mak ng dec s ons of exc ud ng those nva d nstruments or downgrad ng the eve of ev dence).			
Continuous variables are reported or appropriate cut points	The cut off used shou d NOT be based on d str but on of the data, but on estab shed cut offs n the f e d of Wh p ash.			
The method and setting of measurement of PF is the same for all study participants	The PF shou d be the same, but a so cou d be d fferent for d fferent study part c pants f both measures are re ab e (e.g. VAS or NRS when measur ng pa n). However, both nstruments shou d be va d for the use n the f e d of chron c pa n.			
Adequate proportion of the study sample has complete data for PF variable	There shou d be at east 67% ava ab e w th comp ete data. It s mportant a so to check f there s d fferent data ava ab e for d fferent prognost c factors measured s mu taneous y, wh ch cou d nd cate d fferent a oss to fo ow up.			
Appropriate methods of imputation are used for missing 'PF' data	There shou d be some k nd of mputat on, but even f no mputat on was done, t cou d be a 'yes' f at east 67% of the study samp e had comp ete data.			
PF Measurement Summary	***PF is* adequately measured in study participants to sufficiently limit potential bias.**			
4. Outcome Measurement	**Goal: To judge the risk of bias related to the measurement of outcome (differential measurement of outcome related to the baseline level of PF).**			
A clear definition of outcome is provided	There shou d be a c ear def n t on of the outcome measure ava ab e, e.g. how the data was co ected, how the var ab e was measured.			

The method of outcome measurement used is valid and reliable	There shou d be a reference to a re ab ty/va d ty study or nformat on on these features n the paper. Note the popu at on on wh ch the re ab ty/va d ty study was performed shou d correspond to the popu at on of nterest (wh p ash).			
The method and setting of outcome measurement is the same for all study participants	The outcome measures shou d be the same but cou d a so be d fferent for d fferent study part c pants f both measures are re ab e (e.g. VAS or NRS when measur ng pa n). However, both nstruments shou d be va d for the use n the f e d of chron c pa n.			
Outcome Measurement Summary	***Outcome of interest is*** **adequately measured in study participants to sufficiently limit potential bias.**			
5. Study Confounding	**Goal: To judge the risk of bias due to confounding (i.e. the effect of PF is distorted by another factor that is related to PF and outcome).**			
All important confounders are measured	In wh p ash pat ents, at east two of the mportant confounders (age, gender) were measured and are s m ar between part c pants			
Important potential confounders are accounted for in the analysis (i e appropriate adjustment)	In un var ate ana ys s, at east the two confounders are nc uded n the ana ys s			
Study Confounding Summary	**Important potential confounders are appropriately accounted for, limiting potential bias with respect to the relationship between *PF and outcome.***			
6. Statistical Analysis and Reporting	**Goal: To judge the risk of bias related to the statistical analysis and presentation of results.**			
There is sufficient presentation of data to assess the adequacy of the analysis	there shou d be enough nformat on ava ab e to understand the stat st ca methods app ed, so that the rater can determ ne whether the methods used were correct. E.g. un var ate assoc at on must be presented nc ud ng the r est mates			
The selected statistical model is adequate for the design of the study	There shou d be some form of stat st ca ana yses descr pt on ava ab e, resu t ng n nformat on on the effect of the PF on the outcome.			
There is no selective reporting of results	A var ab es (outcomes and PF) that are descr bed n the method sect on shou d be nc uded n the resu t sect on w th words or n numbers (tab es, f gures).			
Statistical Analysis and Presentation Summary	**The statistical analysis is appropriate for the design of the study, limiting potential for presentation of invalid or spurious results.**			

Reference:
Grooten WJ, Tseli E, Äng BO, Boersma K, Stålnacke BM, Gerdle B, Enthoven P. Elaborating on the assessment of the risk of bias in prognostic studies in pain rehabilitation using QUIPS—aspects of interrater agreement. Diagnostic and prognostic research. 2019 Dec 1;3(1):5.

Appendix 17: Description of included studies

Study	Objectives	Inclusion criteria	Exclusion criteria	Recruitment method	Withdrawals	Study dates
(Kasch et al., 2001b)	• To identify the role of possible risk factors and determine the sensitivity and specificity of such factors for predicting which patients will develop late whiplash syndrome	• Involvement in a motor vehicle accident with a rear hit • Preservation of consciousness during collision • No amnesia after the accident • Contact with the local emergency unit within 2 days after trauma with complaints of neck pain or headache • Age between 18 and 70 years	• Previously recorded neck or low-back disorder or head injury • Severe headache, migraine, or widespread pain. • A record of severe psychiatric disease • Known drug or alcohol abuse	• Patients with whiplash injury in the Aarhus area who visited local emergency unit	• Of the 198 individuals remaining after exclusion, 57 subjects did not show up at first examination and 141 were seen at first visit	January 6, 1997 to January 5, 1998
(Atherton et al., 2006)	• To examine the relative contribution of pre-collision health and psychosocial factors, mechanical (that is, collision) factors, and the psychological response to the collision to the	• Aged 17–70 years. • Attending with neck pain within 24 hours of a motor vehicle collision in which they were a driver or passenger • Neck pain was defined as	• Those with a fracture or dislocation of the neck, distracting injury or suspected alcohol or drug intoxication were excluded from the study • Patients who reported an	• During the study period 1500 eligible patients attended the emergency departments and were invited to participate in the study	• Only 765 of eligible patients (1500; response rate 51%) completed a full baseline questionnaire.	1 February 2002 to 30 June 2003

	development of persistent neck pain • To identify those at high risk of persistent symptoms by using information on these factors and the initial post-collision clinical information	pain since the collision, lasting one day or longer, in the area identified in the study	episode of neck pain in the month prior to their collision were also excluded			
(Gun et al., 2005)	• To identify risk factors which may predispose to prolonged disability following whiplash injury using a range of different measures of recovery	• Patients had to present with neck pain as a result of soft-tissue injury following a motor vehicle accident, with no other significant injuries	• Patients with radiologic abnormalities and/or neurologic signs were excluded, as were those with other significant injury (fracture or intracranial, intrathoracic or intra-abdominal injury)	• Patients were recruited from hospital emergency departments and medical and physiotherapy practices • Patients were recruited by the medical practitioners or physiotherapists who examined the patients	• A total of 147 patients were recruited to the study out of 421 originally approached	NR
(Kyhlbäck et al., 2002)	• To investigate the significance and effectiveness of predictors related to disability and pain in WAD patients • To analyse the temporal development of patients' complaints, as studied during the first year after injury	• The combination of acute whiplash injury and an age between 18 and 60 years	• People with poor ability to read the Swedish language • Patients suffering from fractured or dislocated vertebrae or neurological symptoms	• Patients complaining of pain in the neck following acute whiplash injury and scheduled for an appointment with an orthopaedist and a physiotherapist at an orthopaedic clinic were recruited • Eleven patients had previously been	• Ninety-eight patients were consecutively included in the study and 83 eventually participated	January 1997 to May 1998

				exposed to a whiplash injury and four patients sustained another injury during the follow-up period		
(Sterling et al., 2006)	• This study sought to follow up the initial cohort of 76 whiplash injured persons between 2- and 3-years post-motor vehicle crash to determine whether or not the original model maintained its predictive capacity at a long-term follow-up post-whiplash injury	• Participants were eligible if they met the QTF classification of WAD II or III	• Subjects were excluded if they were WAD IV, experienced concussion, loss of consciousness or head injury as a result of the accident and if they reported a previous history of whiplash, neck pain or headaches that required treatment	• Participants were recruited to the study via hospital accident and emergency departments, primary care practices and from advertisement	NR	NR
(Sterling et al., 2005)	• To determine the predictive capacity of the combined comprehensive set of measures (motor, sensory and psychological), encompassing the broad biopsychosocial model of musculoskeletal pain, on outcome (persistent					

	pain and disability) at six months post-whiplash injury					
(Cobo et al., 2010)	• The goal is to identify prognostic factors for poor recovery in whiplash injury after initial evaluation, considering pain as the main variable of the study	• Age between 18-75 • Wad I or II as a result of a road traffic accident with symptoms such as neck pain, headache, or dizziness within 48 hours after injury	• Participants with WAD III or IV • Fractures linked to upper and/or lower extremities • Traumatic brain injury • Cervical spine surgery before injury, and oncologic or rheumatic pathology	NR	NR	October 2005 and June 2007
(Kivioja et al., 2008)	• To investigate the predictive value of the WAD-classification as well as several other factors assessed in the QTF regimen • To investigate if the follow-up program proposed by the QTF improves the outcome	• Age 18–65 • A car accident followed by neck pain less than one week ago • Fluency in the Swedish language	• Previous neck injury. • Other obvious simultaneous injuries or neurological disease	• A consecutive series of 186 patients who were seen in the emergency room within a week from the injury. After that a fracture of the cervical spine had been ruled out by the physician on call, the patients were given an appointment to see an orthopaedic surgeon in the next morning clinic for whiplash injuries	NR	November 1996 and June 1997

(Sterner et al., 2003)	• To describe the incidence of whiplash trauma in a well-defined small-town area and to evaluate different prognostic factors	• All persons seeking medical attention, because of whiplash trauma after a car or a bus accident	• Patients with head injury, unconsciousness, fracture or dislocation of the cervical spine, as well as patients on sick leave due to neck pain were excluded.	• Participants were recruited from the university hospital's emergency room or general practitioners in the community of Umeå.	NR	January 1997 to February 1998)
(Berglund et al., 2006)	• To estimate the influence of potential prognostic factors, i.e. occupant and crash-related factors, initial neck pain intensity and headache, whiplash injury severity, as well as socioeconomic status, helplessness and locus of control on neck pain intensity, disability, anxiety and depression, respectively	• Age 18–65 years • Residents in Sweden • Participants were involved in an MVC, in which at least one car occupant was injured	• Non-Swedish-speaking, early disability pension, comorbidity, or pregnancy	• Data for this report were obtained from claim reports	Not applicable	September 1, 1993 to August 31, 1994
(Hartling et al., 2001)	• To evaluate the utility of the classification as an initial assessment tool • To assess its ability to predict whether these patients continued to experience	• 18 years or older • Involved in a rear-end MVC, in which their vehicle was hit from behind • Presenting for emergency care for	• Patients diagnosed with a fracture, dislocation or subluxation of the vertebrae • Injury to the spinal cord, or head injury	• Participants were recruited from two emergency departments.	NR	October 1, 1995 and March 31, 1998

	symptoms of WAD at various intervals post collision • To examine one potential modification to the QTF classification system	the first time for the injury in question				
(Sterling et al., 2012)	• To externally validate a previously developed predictive model for poor functional recovery after whiplash injury.	• Included if they met the Quebec Task Force Classification of whiplash grades I, II or III.	• WAD IV (fracture or dislocation) • Experienced concussion, loss of consciousness or head injury as a result of the accident. • A history of whiplash, neck pain or headaches that required treatment.	• Consecutive participants were recruited from primary care practices (medical and physiotherapy) and accident and emergency departments of local hospitals, and through general advertisement.	NR	• 2005 to 2008
(Ritchie et al., 2013)	• To analyse previously identified predictor variables of poor recovery for inclusion within a CPR • To derive a dual-pathway CPR for whiplash injury that ensured an acceptable revised percentage (PPV) of those predicted to develop chronic moderate/severe	• Individuals with acute whiplash following a motor vehicle crash with Quebec Task Force Classification of WAD I, II, or III.	• WAD IV (fracture or dislocation) • Experienced concussion or head injury as a result of the accident • A previous history of whiplash, neck pain, or headaches that required treatment. They were also excluded • Diagnosed with or receiving treatment for a	NR	NR	• 2006 to 2010

	symptoms or to recover fully.		psychiatric or psychological condition either currently or in the past.			
(Hours et al., 2014)	• To compare the various consequences of a mild accident at 12 months of follow-up in terms of symptomatology, and familial, social, and occupational disturbances, and the effect on QOL between whiplash casualties versus other mild injury casualties. • To determine whether whiplash is a prognostic factor for poorer QOL at 12 months after the accident.	• Adults in the ESPARR cohort who had sustained only mild injury, defined as a maximum AIS grade 1 (MAIS1). • All subjects with lesions classified as cervical contusion or neck sprain were considered whiplash casualties.	• Cases of 1 or more associated AIS ≥ 2 lesions in different body regions.	• At inclusion, the registry's experienced physician codes all lesions according to the Abbreviated Injury Scale (AIS) criteria1, working from the initial medical records, which cover symptomatology, clinical, and biological examination results and imaging were judged necessary. Each elementary lesion is thus coded, as is severity on a scale from 1 (minor) to 6 (maximal).	NR	• October 2004 to December 2005
QTF: Quebec Task Force; WAD: Whiplash-associated disorder						

Appendix 18: Number of participants at each follow-up timepoint

Study	Baseline Number	Follow-up 3 m	Follow-up 6 m	Follow-up 12 m	Follow-up 16 m	Follow-up 18 m	Follow-up 24 m	Follow-up 2-3 years
(Kasch et al., 2001b)	141							
(Atherton et al., 2006)	765			480				
(Gun et al., 2005)	147			135				
(Kyhlbäck et al., 2002)	83	68		70				
(Kivioja et al., 2008)	91			86				
(Sterling et al., 2006)	76							65
(Sterling et al., 2005)	76		76					
(Sterner et al., 2003)	356				296			
(Hartling et al., 2001)	380		334	247		176	126	
(Berglund et al., 2006)	2280		1391	1349			1381	
(Cobo et al., 2010)	682		557					
(Sterling et al., 2012)	286			225				
(Ritchie et al., 2013)	262			195				
(Hours et al., 2014)	253			171				

Appendix 19: List of excluded studies with the reason of exclusion

	Title of the study	Published Year	Reason for exclusion
1.	Trajectories of posttraumatic stress symptoms after whiplash: A prospective cohort study	2019	Has no predictor or outcome of interest
2.	Differences in the kinematics of the cervical and thoracic spine during functional movement in individuals with or without chronic neck pain: a systematic review	2019	Not a cohort or prognostic study
3.	Cervical Rotator Muscle Activity With Eye Movement at Different Speeds is Distorted in Whiplash	2019	Not a cohort or prognostic study
4.	A 20-year prospective longitudinal MRI study on cervical spine after whiplash injury: Follow-up of a cross-sectional study	2019	Has no predictor or outcome of interest
5.	MRI signs of brachial plexus and median nerve inflammation and morphological changes in chronic whiplash associated disorder	2019	Has no predictor or outcome of interest
6.	Instant reduction in postural sway during quiet standing by intraoral dental appliance in patients with Whiplash associated Disorders and non-trauma neck pain	2019	Patients with chronic whiplash
7.	Clinical assessment of cervical movement sense in those with neck pain compared to asymptomatic individuals	2019	Patients with chronic whiplash
8.	Deep Learning Convolutional Neural Networks for the Automatic Quantification of Muscle Fat Infiltration Following Whiplash Injury	2019	Wrong or incomplete definition of population
9.	Cross-sectional and Prospective Correlates of Recovery Expectancies in the Rehabilitation of Whiplash Injury	2018	Patients with chronic whiplash
10.	Association Between Clinical and Neurophysiological Outcomes in Patients With Mechanical Neck Pain and Whiplash-associated Disorders	2018	Patients with chronic whiplash
11.	Lateral atlantoaxial joint meniscoid volume in individuals with whiplash associated disorder: A case-control study	2018	Not a cohort or prognostic study

12.	Women with late whiplash syndrome have greatly reduced load-bearing of the cervical spine. In-vivo biomechanical, cross-sectional, lateral radiographic study	2018	Patients with chronic whiplash
13.	Alterations in the Mechanical Response of Deep Dorsal Neck Muscles in Individuals Experiencing Whiplash-Associated Disorders Compared to Healthy Controls: An Ultrasound Study	2018	Patients with chronic whiplash
14.	Long-term follow-up of whiplash injuries reported to insurance companies: a cohort study on patient-reported outcomes and impact of financial compensation	2018	Has no predictor or outcome of interest
15.	The qualitative grading of muscle fat infiltration in whiplash using fat and water magnetic resonance imaging	2018	Patients with chronic whiplash
16.	Relationship between neck motion and self-reported pain in patients with whiplash associated disorders during the acute phase	2018	Patients with chronic whiplash
17.	Short- and long-term reproducibility of diffusion-weighted magnetic resonance imaging of lower extremity musculature in asymptomatic individuals and a comparison to individuals with spinal cord injury	2018	Wrong or incomplete definition of population
18.	Physical examination of dizziness in athletes after a concussion: A descriptive study	2018	Wrong or incomplete definition of population
19.	Predictors before and after multimodal rehabilitation for pain acceptance and engagement in activities at a 1-year follow-up for patients with whiplash-associated disorders (WAD), a study based on the Swedish Quality Registry for Pain Rehabilitation (SQRP)	2018	Has no predictor or outcome of interest
20.	Interdisciplinary rehabilitation after whiplash injury: An observational prospective 5 years outcome study	2017	Patients with chronic whiplash
21.	Traumatic sports-related cervical spine injuries	2017	Part of RCT

22.	Eye movements in patients with Whiplash Associated Disorders: a systematic review	2016	Not a cohort or prognostic study
23.	Ultrasonographic analysis of dorsal neck muscles thickness changes induced by isometric contraction of shoulder muscles: A comparison between patients with chronic neck pain and healthy controls	2016	Wrong or incomplete definition of population
24.	Postural stability in patients with different types of head and neck trauma in comparison to healthy subjects	2016	Wrong or incomplete definition of population
25.	The long-term course of deficient cervical kinaesthesia following a whiplash injury has a tendency to seek a physiological homeostasis. A prospective study	2016	Patients with chronic whiplash
26.	MicroRNA 320a predicts chronic axial and widespread pain development following motor vehicle collision in a stress-dependent manner	2016	Has no predictor or outcome of interest
27.	Risk factors for chronic disability in a cohort of patients with acute whiplash associated disorders seeking physiotherapy treatment for persisting symptoms	2015	Part of RCT
28.	The rapid and progressive degeneration of the cervical multifidus in whiplash: A MRI study of fatty infiltration	2015	Has no predictor or outcome of interest
29.	Associations with legal representation in a compensation setting 12 months after injury	2015	Patients with chronic whiplash
30.	A prospective study of perceived injustice in whiplash victims and its relationship to recovery	2015	Has no predictor or outcome of interest
31.	Whiplash: are you at risk for ongoing pain or disability?	2015	Not a cohort or prognostic study
32.	Predictors of outcome following a short multimodal rehabilitation program for patients with whiplash associated disorders	2015	Patients with chronic whiplash
33.	Smooth Pursuit Eye Movement Deficits in Patients With Whiplash and Neck Pain are Modulated by Target Predictability	2015	Patients with chronic whiplash

34.	Altered ventral neck muscle deformation for individuals with whiplash associated disorder compared to healthy controls e A case-control ultrasound study	2015	Not a cohort or prognostic study
35.	Multidimensional associative factors for improvement in pain, function, and working capacity after rehabilitation of whiplash associated disorder: a prognostic, prospective outcome study	2014	Patients with chronic whiplash
36.	Postural stability in subjects with whiplash injury symptoms: results of a pilot study	2014	Patients with chronic whiplash
37.	Properties of patient-reported outcome measures in individuals following acute whiplash injury	2014	Not a cohort or prognostic study
38.	Relationship between self-reported disability and functional capacity in patients with whiplash associated disorder	2014	Patients with chronic whiplash
39.	Whiplash evokes descending muscle recruitment and sympathetic responses characteristic of startle	2014	Wrong or incomplete definition of population
40.	Symptoms, disabilities, and life satisfaction five years after whiplash injuries	2014	Patients with chronic whiplash
41.	A new stratified risk assessment tool for whiplash injuries developed from a prospective observational study	2013	Part of RCT
42.	Outcomes at 12 months after early magnetic resonance imaging in acute trauma patients with persistent midline cervical tenderness and negative computed tomography	2013	Wrong or incomplete definition of population
43.	Quantification of cervical spine muscle fat: a comparison between T1-weighted and multi-echo gradient echo imaging using a variable projection algorithm (VARPRO)	2013	Wrong or incomplete definition of population
44.	Coping patterns and their relation to daily activity, worries, depressed mood, and pain intensity in acute whiplash-associated disorders	2013	Has no predictor or outcome of interest
45.	Sensorimotor incongruence exacerbates symptoms in patients with chronic whiplash associated disorders: an experimental study	2012	Patients with chronic whiplash

46.	The value of cervical magnetic resonance imaging in the evaluation of the obtunded or comatose patient with cervical trauma, no other abnormal neurological findings, and a normal cervical computed tomography	2012	Wrong or incomplete definition of population
47.	Persistent neck pain after motor vehicle collision	2012	Not a cohort or prognostic study
48.	Reproducibility of the cervical range of motion (CROM) device for individuals with sub-acute whiplash associated disorders	2012	Not a cohort or prognostic study
49.	Upper cervical spine kinematic response and injury prediction	2012	Wrong or incomplete definition of population
50.	Cervico-ocular coordination during neck rotation is distorted in people with whiplash-associated disorders	2011	Patients with chronic whiplash
51.	Relationship Between Pressure Pain Thresholds and Pain Ratings in Patients With Whiplash-associated Disorders	2011	Has no predictor or outcome of interest
52.	The risk assessment score in acute whiplash injury predicts outcome and reflects biopsychosocial factors	2011	Has no predictor or outcome of interest
53.	Neck motion patterns in whiplash-associated disorders: quantifying variability and spontaneity of movement	2011	Patients with chronic whiplash
54.	Predictors of neck pain after motor vehicle collisions: a prospective survey	2011	Has no predictor or outcome of interest
55.	Dizziness among patients with whiplash-associated disorder -- a randomized controlled trial	2011	Not a cohort or prognostic study
56.	Characterization of postural control deficit in whiplash patients by means of linear and nonlinear analyses - A pilot study	2011	Patients with chronic whiplash
57.	Reduced force steadiness in women with neck pain and the effect of short term vibration	2011	Wrong or incomplete definition of population
58.	Dynamic and functional balance tasks in subjects with persistent whiplash: a pilot trial	2011	Patients with chronic whiplash

59.	Influence of whiplash injury on cervical spine stability	2011	Has no predictor or outcome of interest
60.	Cognitive symptoms, cervical range of motion and pain as prognostic factors after whiplash trauma	2010	Has no predictor or outcome of interest
61.	Are MRI high-signal changes of alar and transverse ligaments in acute whiplash injury related to outcome?	2010	Has no predictor or outcome of interest
62.	Use of muscle functional magnetic resonance imaging to compare cervical flexor activity between patients with whiplash-associated disorders and people who are healthy	2010	Patients with chronic whiplash
63.	The course of symptoms for whiplash-associated disorders in Sweden: 6-month follow-up study	2010	Has no predictor or outcome of interest
64.	Prospective ten-year follow-up study comparing patients with whiplash-associated disorders and asymptomatic subjects using magnetic resonance imaging	2010	Has no predictor or outcome of interest
65.	Magnetic resonance imaging findings of fatty infiltrate in the cervical flexors in chronic whiplash	2010	Patients with chronic whiplash
66.	Differentiating malingering balance disorder patients from healthy controls, compensated unilateral vestibular loss, and whiplash patients using stance and gait posturography	2010	Patients with chronic whiplash
67.	Whiplash-associated disorders affect postural reactions to antero-posterior support surface translations during sitting	2009	Patients with chronic whiplash
68.	Clinical assessment of prognostic factors for long-term pain and handicap after whiplash injury: a 1-year prospective study	2008	Part of RCT
69.	Deep muscle pain, tender points and recovery in acute whiplash patients: A 1-year follow-up study	2008	Part of RCT
70.	Are early MRI findings correlated with long-lasting symptoms following whiplash injury? A prospective trial with 1-year follow-up	2008	Part of RCT
71.	Are altered smooth pursuit eye movements related to chronic pain and disability following whiplash	2008	Part of RCT

	injuries? A prospective trial with one-year follow-up		
72.	Acute stress response and recovery after whiplash injuries. A one-year prospective study	2008	Has no predictor or outcome of interest
73.	Can long-term impairment in general practitioner whiplash patients be predicted using screening and patient-reported outcomes?	2008	Has no predictor or outcome of interest
74.	Self-reported driving habits in subjects with persistent whiplash-associated disorder: relationship to sensorimotor and psychologic features	2008	Patients with chronic whiplash
75.	Functional health status in subjects after a motor vehicle accident, with emphasis on whiplash associated disorders: design of a descriptive, prospective inception cohort study	2008	Not a cohort or prognostic study
76.	Quality of life in subgroups of individuals with whiplash associated disorders	2008	Patients with chronic whiplash
77.	Fatty infiltrate in the cervical extensor muscles is not a feature of chronic, insidious-onset neck pain	2008	Patients with chronic whiplash
78.	Consciously postural sway and cervical vertigo after whiplash injury	2008	Patients with chronic whiplash
79.	Standing balance: a comparison between idiopathic and whiplash-induced neck pain	2008	Patients with chronic whiplash
80.	Are cervical multifidus muscles active during whiplash and startle? An initial experimental study	2008	Not a cohort or prognostic study
81.	Clinical assessment techniques for detecting ligament and membrane injuries in the upper cervical spine region-A comparison with MRI results	2008	Wrong or incomplete definition of population
82.	Neck Collar,“Act-as-Usual” or Active Mobilization for Whiplash Injury?: A Randomized Parallel-Group Trial	2007	Part of RCT
83.	The correlation between surgical and fMRI findings after trauma to the upper cervical spine	2007	Wrong or incomplete definition of population

84.	Active range of motion as an indicator for ligament and membrane lesions in the upper cervical spine after a whiplash trauma	2007	Has no predictor or outcome of interest
85.	Jaw-neck dysfunction in whiplash-associated disorders	2007	Has no predictor or outcome of interest
86.	Neck muscle fatigue and postural control in patients with whiplash injury	2006	Patients with chronic whiplash
87.	Fatty infiltration in the cervical extensor muscles in persistent whiplash-associated disorders: a magnetic resonance imaging analysis	2006	Patients with chronic whiplash
88.	Head repositioning accuracy in patients with whiplash-associated disorders	2006	Wrong or incomplete definition of population
89.	Whiplash injuries can be visible by functional magnetic resonance imaging	2006	Not a cohort or prognostic study
90.	A prospective cohort study of health outcomes following whiplash associated disorders in an Australian population	2006	Patients with chronic whiplash
91.	Cervical vertigo and dizziness after whiplash injury	2006	Wrong or incomplete definition of population
92.	Factors predicting outcome after whiplash injury in subjects pursuing litigation	2006	Wrong or incomplete definition of population
93.	Prognostic factors for poor recovery in acute whiplash patients	2005	Part of RCT
94.	Measurement of cervical flexor endurance following whiplash	2005	Not a cohort or prognostic study
95.	Reduced cold pressor pain tolerance in non-recovered whiplash patients: a 1-year prospective study	2005	Has no predictor or outcome of interest
96.	The cervico-ocular reflex is increased in whiplash injury patients	2005	Patients with chronic whiplash
97.	Turning away from whiplash. An EMG study of head rotation in whiplash impact	2005	Wrong or incomplete definition of population
98.	Cervical muscle response to trunk flexion in whiplash-type lateral impacts	2005	Wrong or incomplete definition of population

99.	Standing balance in persistent whiplash: a comparison between subjects with and without dizziness	2005	Patients with chronic whiplash
100.	Correlation of clinical findings, collision parameters, and psychological factors in the outcome of whiplash associated disorders	2004	Has no predictor or outcome of interest
101.	Whiplash injuries in Finland - the possibility of some sociodemographic and psychosocial factors to predict the outcome after one year	2004	Has no predictor or outcome of interest
102.	Impairment in the cervical flexors: a comparison of whiplash and insidious onset neck pain patients	2004	Patients with chronic whiplash
103.	Segmental vertebral motion in the assessment of neck range of motion in whiplash patients	2004	Patients with chronic whiplash
104.	Control subjects in whiplash studies...responses to a clinical test of mechanical provication of nerve tissue in whiplash associated disorder. Manual Therapy 7: 89-94	2003	Not a cohort or prognostic study
105.	Acute peripheral vestibular deficits after whiplash injuries	2003	Not a cohort or prognostic study
106.	Whiplash associated disorder in children attending the emergency department	2002	Wrong or incomplete definition of population
107.	Prediction of outcome in whiplash-associated disorders using West Haven-Yale Multidimensional Pain Inventory	2002	Has no predictor or outcome of interest
108.	Derivation of a clinical decision rule for whiplash associated disorders among individuals involved in rear-end collisions	2002	Has no predictor or outcome of interest
109.	Whiplash injury sustained in motor vehicle accidents: factors influencing time off work	2001	Has no predictor or outcome of interest
110.	Prospective study of trigeminal sensibility after whiplash trauma	2001	Patients with chronic whiplash
111.	Risk factors for long-term treatment of whiplash injury in Japan: analysis of 400 cases	2001	Has no predictor or outcome of interest
112.	The association between exposure to a rear-end collision and future health complaints	2001	Has no predictor or outcome of interest

113.	Headaches in the whiplash syndrome	2001	Has no predictor or outcome of interest
114.	Cervical range of motion discriminates between asymptomatic persons and those with whiplash	2001	Patients with chronic whiplash
115.	Balance performance in patients with whiplash associated disorders and patients with prolonged musculoskeletal disorders	2001	Patients with chronic whiplash
116.	Acute whiplash-associated disorders (WAD): the effects of early mobilization and prognostic factors in long-term symptomatology	2000	Part of RCT
117.	WHIPLASH INJURY-ARE CURRENT HEAD RESTRAINTS DOING THEIR JOB?	2000	Has no predictor or outcome of interest
118.	The association between exposure to a rear-end collision and future neck or shoulder pain: A cohort study	2000	Has no predictor or outcome of interest
119.	Whiplash injuries from car accidents in a Swedish middle-sized town during 1993-95	2000	Has no predictor or outcome of interest
120.	Cervical muscle response during whiplash: evidence of a lengthening muscle contraction	2000	Not a cohort or prognostic study
121.	Deep cervical flexor muscle dysfunction in whiplash	2000	Patients with chronic whiplash
122.	A prospective study of acceleration-extension injuries following rear-end motor vehicle collisions	1999	Wrong or incomplete definition of population
123.	Pain after whiplash: a prospective controlled inception cohort study	1999	Has no predictor or outcome of interest
124.	Imaging traumatic and nontraumatic neck emergencies in the adult	1999	Not a cohort or prognostic study
125.	Evaluation of balance disorders during the first month after whiplash injury	1998	Not a cohort or prognostic study
126.	An examination of reasons for prolonged treatment in Japanese patients with whiplash injuries	1997	Has no predictor or outcome of interest
127.	A prospective study of 39 patients with whiplash injury	1997	Has no predictor or outcome of interest

128.	MRI of car occupants with whiplash injury	1997	Has no predictor or outcome of interest
129.	Disc pathology after whiplash injury. A prospective magnetic resonance imaging and clinical investigation	1997	Has no predictor or outcome of interest
130.	Long-term outcome of motor vehicle accident injury	1997	Has no predictor or outcome of interest
131.	MRI of cerebrum and cervical columna within two days after whiplash neck sprain injury	1997	Has no predictor or outcome of interest
132.	Personality profile among symptomatic and recovered patients with neck sprain injury, measured by MCMI-I acutely and 6 months after car accidents	1997	Has no predictor or outcome of interest
133.	Ability to reproduce head position after whiplash injury	1997	Patients with chronic whiplash
134.	Functional brain imaging in 200 patients after whiplash injury	1997	Not a cohort or prognostic study
135.	Predicting recovery from common whiplash	1996	Has no predictor or outcome of interest
136.	The relationship between cervical whiplash and temporomandibular joint injuries: an MRI study	1996	Has no predictor or outcome of interest
137.	Outcome of 'whiplash' neck injury	1996	Incomplete information of physical factor definition
138.	Prolonged functional impairment after whiplash injury	1996	Patients with chronic whiplash
139.	Whiplash injuries: Is there a role for imaging?	1996	Patients with chronic whiplash
140.	Disturbed eye movements after whiplash due to injuries to the posture control system	1996	Patients with chronic whiplash
141.	Acute Emotional Response to Common Whiplash Predicts Subsequent Pain Complaints - a Prospective-Study of 107 Subjects Sustaining Whiplash Injury	1995	Has no predictor or outcome of interest
142.	MR imaging and radiography of patients with cervical	1995	Has no predictor or outcome of interest

	hyperextension-flexion injuries after car accidents		
143.	MRI in acute phase of whiplash injury	1995	Has no predictor or outcome of interest

Appendix 20: STROBE Statement—Checklist of items that should be included in reports of *cross-sectional studies*

	Item No	Recommendation	Page No
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	1
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	1
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	1-2
Objectives	3	State specific objectives, including any prespecified hypotheses	1
Methods			
Study design	4	Present key elements of study design early in the paper	1
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	3-5
Participants	6	(*a*) Give the eligibility criteria, and the sources and methods of selection of participants	3-4
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	4,7-9
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	5-7
Bias	9	Describe any efforts to address potential sources of bias	NA
Study size	10	Explain how the study size was arrived at	9
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	9
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	9
		(*b*) Describe any methods used to examine subgroups and interactions	NA
		(*c*) Explain how missing data were addressed	10
		(*d*) If applicable, describe analytical methods taking account of sampling strategy	NA
		(*e*) Describe any sensitivity analyses	NA
Results			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	10, 13
		(b) Give reasons for non-participation at each stage	13
		(c) Consider use of a flow diagram	3
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	10
		(b) Indicate number of participants with missing data for each variable of interest	13
Outcome data	15*	Report numbers of outcome events or summary measures	13
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	NA
		(*b*) Report category boundaries when continuous variables were categorized	NA

		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	NA
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	NA
Discussion			
Key results	18	Summarise key results with reference to study objectives	15
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	18-19
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	15-18
Generalisability	21	Discuss the generalisability (external validity) of the study results	18-19
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	19

Appendix 21: Summary of amendments submitted to ethical review committee for Chapter Five

Ethical application	Reference	Changes
Original ethics application	ERN_19-0564	-
First amendments	ERN_19-0564A	This amendment will provide more information regarding the recruitment method that will be used to increase the recruitment rate, specially of those with recurrent neck pain initiated following a whiplash trauma. This change is deemed necessary as recruitment has progressed slower than expected and in particular, we have struggled to identify sufficient people with a past history of a whiplash injury and we believe that the advertisement did sufficiently specify that we were seeking to recruit such people. To facilitate recruitment we propose: Participants will be included if they will report at least two episodes of neck pain (lasting more than 24 hours) separated by periods of remission during the last 12 months. In the approved original application, the previous remission days were 30 days, but after initial tests we deemed it important to decrease the number to 10 days to facilitate recruitment. Adjusting recruitment information to accurately reflect the need of those who have recurrent neck pain originating as a result of a whiplash trauma. The original flyer will be maintained, and an additional flyer has been included in this amendment which specifically targets those that have sustained a whiplash injury. Post an ad on social media including Facebook and our established twitter account at CPR Spine. This recruitment information will be posted passively (not as paid-for adverts) on social media websites including Facebook and Twitter. These posts will be visible to anybody who views or subscribes to the accounts but will not be posted excessively or onto a page or group where it is not appropriate Post ad advert in a local newspaper (Harborne, Edgbaston & Moseley - https://issuu.com/philby176/docs/hem-life-october-2019)

		Place the approved recruitment flyers in private physiotherapy practices in the local area of Birmingham following approval from practice owners. This will only be presented at private practices and therefore not advertised to NHS patients.
Second amendments	ERN_19-0564B	In the last amendments application (ERN_19-0564A), we requested that we need to add more recruitment method in order to increase the number of participants who have recurrent neck pain initiated following a whiplash trauma. Unfortunately, the previous adopted recruitment strategies did not improve the recruitment rate and we still struggle to identify sufficient people with a past history of a whiplash injury. Therefore, we would like to expand our recruitment strategy to include a paid Facebook post. The advert will be restricted and in order for it to be visible to specific user, three conditions have to be met: The user must live withing 10 km of the University of Birmingham campus. A user has to search in Facebook search bar using specific search terms, such as 'whiplash injury', 'neck pain', or 'car accident'. Their age between 25 and 50 years old Unless all three conditions are met, Facebook users will not see the advert. The advert will be live until we reach the required sample size.

Appendix 22: Ethical approval

Thursday, September 15, 2022 at 08:32:53 British Summer Time

Subject: FW: Application for Ethical Review ERN_19-0564
Date: Thursday, 15 September 2022 at 8:30:13 am British Summer Time
From: Ahmed Alalawi (PhD School of Sprt+Ex Scie FT)
To: Ahmed Alalawi (PhD School of Sprt+Ex Scie FT)
Attachments: image001.jpg

UNIVERSITY OF BIRMINGHAM | CENTRE OF PRECISION REHABILITATION FOR SPINAL PAIN

From: Samantha Waldron
Sent: 10 June 2019 15:45
To: Deborah Falla
Cc: Valter Devecchi
Subject: Application for Ethical Review ERN_19-0564

Dear Professor Deborah Falla,

Re: "Neuromuscular adaptations in people with recurrent neck pain during a period of remission"
Application for Ethical Review ERN_19-0564

Thank you for your application for ethical review for the above project, which was reviewed by the Science, Technology, Engineering and Mathematics Ethical Review Committee.

On behalf of the Committee, I confirm that this study now has full ethical approval.

I would like to remind you that any substantive changes to the nature of the study as described in the Application for Ethical Review, and/or any adverse events occurring during the study should be promptly brought to the Committee's attention by the Principal Investigator and may necessitate further ethical review.

Please also ensure that the relevant requirements within the University's Code of Practice for Research and the information and guidance provided on the University's ethics webpages (available at https://intranet.birmingham.ac.uk/finance/accounting/Research-Support-Group/Research-Ethics/Links-and-Resources.aspx) are adhered to and referred to in any future applications for ethical review. It is now a requirement on the revised application form (https://intranet.birmingham.ac.uk/finance/accounting/Research-Support-Group/Research-Ethics/Ethical-Review-Forms.aspx) to confirm that this guidance has been consulted and is understood, and that it has been taken into account when completing your application for ethical review.

Please be aware that whilst Health and Safety (H&S) issues may be considered during the ethical review process, you are still required to follow the University's guidance on H&S and to ensure that H&S risk assessments have been carried out as appropriate. For further information about this, please contact your School H&S representative or the University's H&S Unit at healthandsafety@contacts.bham.ac.uk.

Kind regards,

Ms Sam Waldron
Deputy Research Ethics Officer

Appendix 23: Ethical approval (First Amendment approval)

UNIVERSITY OF BIRMINGHAM | CENTRE OF PRECISION REHABILITATION FOR SPINAL PAIN

From: Susan Cottam [redacted]
Sent: 03 September 2019 11:13
To: Deborah Falla [redacted]
Subject: Application for amendment ERN_19-0564A

Dear Professor Falla

Re: "Neuromuscular adaptations in people with recurrent neck pain during a period of remission"
Application for amendment ERN_19-0564A

Thank you for the above application for amendment, which was reviewed by the Science, Technology, Engineering and Mathematics Ethical Review Committee.

On behalf of the Committee, I can confirm that this amendment now has full ethical approval.

I would like to remind you that any substantive changes to the nature of the study as now amended, and/or any adverse events occurring during the study should be promptly brought to the Committee's attention by the Principal Investigator and may necessitate further ethical review. A revised amendment application form is now available at https://intranet.birmingham.ac.uk/finance/accounting/Research-Support-Group/Research-Ethics/Ethical-Review-Forms.aspx . Please ensure this form is submitted for any further amendments.

Please also ensure that the relevant requirements within the University's Code of Practice for Research and the information and guidance provided on the University's ethics webpages (available at https://intranet.birmingham.ac.uk/finance/accounting/Research-Support-Group/Research-Ethics/Links-and-Resources.aspx) are adhered to and referred to in any future applications for ethical review. It is now a requirement on the revised application form (https://intranet.birmingham.ac.uk/finance/accounting/Research-Support-Group/Research-Ethics/Ethical-Review-Forms.aspx) to confirm that this guidance has been consulted and is understood, and that it has been taken into account when completing your application for ethical review.

Please be aware that whilst Health and Safety (H&S) issues may be considered during the ethical review process, you are still required to follow the University's guidance on H&S and to ensure that H&S risk assessments have been carried out as appropriate. For further information about this, please contact your School H&S representative or the University's H&S Unit at healthandsafety@contacts.bham.ac.uk.

If you require a hard copy of this correspondence, please let me know.

Kind regards

Susan Cottam
Research Ethics Manager
[redacted]

Appendix 24: Ethical approval (Second amendment approval)

Subject: FW: Application for Ethical Review ERN_19-0564B
Date: Wednesday, 14 September 2022 at 3:14:52 pm British Summer Time
From: Deborah Falla (Sport, Exercise and Rehabilitation Sciences)
To: Ahmed Alalawi (PhD School of Sprt+Ex Scie FT)
Attachments: image001.jpg

From: Susan Cottam [redacted]
Sent: 21 July 2020 17:55
To: Deborah Falla (Sport, Exercise and Rehabilitation Sciences) [redacted]
Cc: Alison Rushton (Sport, Exercise and Rehabilitation Sciences) [redacted]; Nicola Heneghan (Physiotherapy) [redacted] 'Alessandro De Nunzio [redacted] Eduardo Martinez Valdes (Sport, Exercise and Rehabilitation Sciences) [redacted] Valter Devecchi (PhD School of Sprt+Ex Scie FT) [redacted] Ahmed Alalawi (PhD School of Sprt+Ex Scie FT) [redacted]
Subject: Application for Ethical Review ERN_19-0564B

Dear Professor Falla

Re: "Neuromuscular adaptations in people"
Application for Ethical Review ERN_19-0564B

Thank you for the above application for amendment, which was reviewed by the Science, Technology, Engineering and Mathematics Ethical Review Committee.

On behalf of the Committee, I can confirm that this amendment now has full ethical approval.

I would like to remind you that any substantive changes to the nature of the study as now amended, and/or any adverse events occurring during the study should be promptly brought to the Committee's attention by the Principal Investigator and may necessitate further ethical review. A revised amendment application form is now available at https://intranet.birmingham.ac.uk/finance/accounting/Research-Support-Group/Research-Ethics/Ethical-Review-Forms.aspx . Please ensure this form is submitted for any further amendments.

Please also ensure that the relevant requirements within the University's Code of Practice for Research and the information and guidance provided on the University's ethics webpages (available at https://intranet.birmingham.ac.uk/finance/accounting/Research-Support-Group/Research-Ethics/Links-and-Resources.aspx) are adhered to and referred to in any future applications for ethical review. It is now a requirement on the revised application form (https://intranet.birmingham.ac.uk/finance/accounting/Research-Support-Group/Research-Ethics/Ethical-Review-Forms.aspx) to confirm that this guidance has been consulted and is understood, and that it has been taken into account when completing your application for ethical review.

Please be aware that whilst Health and Safety (H&S) issues may be considered during the ethical review process, you are still required to follow the University's guidance on H&S and to ensure that H&S risk assessments have been carried out as appropriate. For further information about this, please contact your School H&S representative or the University's H&S Unit at healthandsafety@contacts.bham.ac.uk.

If you require a hard copy of this correspondence, please let me know.

Kind regards

Susan Cottam

Appendix 25: Participant information sheet for people with recurrent neck pain

UNIVERSITY OF BIRMINGHAM | CENTRE OF PRECISION REHABILITATION FOR SPINAL PAIN

Neuromuscular adaptations in people with recurrent neck pain during a period of remission

We are looking for volunteers to take part in a research study. Before you decide whether you would like to take part, it is important that you know what the study is about and what it would involve for you. This is explained below; please read the information carefully.

WHAT IS THE STUDY ABOUT?

Research has shown that movement and muscle activity is altered in people with chronic neck pain. What is not known, is whether neck muscle activity and coordination in people with recurrent neck pain (painful episodes followed by asymptomatic periods) are altered and if ongoing alterations in muscle function could negatively influence the ongoing nature of pain. Therefore, the main purpose of the study is to investigate neck muscle activity and movement in people with recurrent neck pain, then data will be compared with healthy volunteers and people with chronic neck pain with current symptoms.

CAN I PARTICIPATE?

You can participate if you meet the following criteria:

- Have had a prior whiplash injury;
- Age between 18 and 65 years;
- Have had 2 or more neck pain episodes over the last year;
- Pain episodes lasted 24 hours or more;
- Pain-free over the last 10 days;

You must also ***not*** fall in any of the categories below:

previous spinal or shoulder surgery, neck or shoulder injury that resulted in a fracture, current neuropathies/radiculopathies, neurological deficits, rheumatic condition, pregnancy.

We will ask you to complete a brief screening assessment to ensure you are eligible to participate. This will be performed by an experienced researcher and will include questions about your general health and LBP.

WHAT WILL I HAVE TO DO IF I PARTICIPATE?

We will ask that you to attend one data collection session, taking approximately 2 hours, this session can be organised at a time that will suit you. During these sessions, we will analyse your neck movements (flexion, extension, and rotation) and the activity of your cervical muscles by surface electromyography. At first, in order to analyse movement, fitted elastic straps will be used to place inertial measurement units on your forehead and over your back. An inertial measurement unit is a wearable sensor similar to a little box (dimensions of approximately 5x4x2 cm). Then, during the second part of the experiment, we will place surface electrodes (like ECG electrodes) on your skin to record the activity of your neck muscles and we will ask you to perform static contractions. We will ask you to bring a top for this session in order to perform movements in a comfortable way. The experiment will take place in the CPR Spine labs.
Furthermore, over the course of 12 months, we will ask you to fill out and submit an additional electronic questionnaire once a month. We will use it to collect data about the recurrence of painful episodes.

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HOW MUCH TIME WILL I HAVE TO SPEND IN TOTAL?

The screening assessment and questionnaires will require approximately 20-30 minutes. Data collection in the lab will last approximately 2 hours. Questionnaires will cover the following topics: neck pain and disability, physical activity, fear of movement and health related quality of life.

ARE THERE ANY BENEFITS FOR ME IF I TAKE PART?

You will gain a better understanding of your neck movement how your neck muscles activate and how this may be linked to recurrent painful episodes.

ARE THERE ANY RISKS FOR ME IF I TAKE PART?

The risks are low, as all procedures are carried out by experienced professionals and you will be thoroughly screened to ensure that it is safe for you to take part. All tests performed are non-invasive. You may experience discomfort, or dizziness during repeated neck movements. You may also feel discomfort and fatigue during the muscle contractions. If, however you feel any discomfort or pain during any aspect of the study, then you will be free to stop and should you wish, you can withdraw from the study.

ARE THERE ANY COST OR REIMBURSEMENTS FOR ME?

There is no cost for this study, but you will be compensated £15 for attending the full laboratory session. If you choose to withdraw during this session, you will be offered partial compensation which is determined by the amount of time that you were was present in the Lab before withdrawal. Moreover, you will receive an additional £5 per monthly questionnaire completed for an additional £60 if all 12 monthly questionnaires are completed. Finally, if all 12 questionnaires are completed you will receive a further £20. Thus the maximum of £95 will be provided upon completion of the study. Payments will be made after each session/questionnaire if you prefer or you can receive one full payment at the end.

DO I HAVE TO TAKE PART?

No, participation is entirely voluntary. If you decide to take part but you change your mind, you can withdraw from the study at any point and up to two weeks following completion of data collection in the laboratory without having to give a reason.

WILL MY DATA BE KEPT CONFIDENTIAL?

All information collected on you will be kept strictly confidential. The consent form containing your allocated ID will never be present in electronic form, will be securely stored within CPR Spine and only available to the researchers. All data will be stored for 10 years managed in accordance with the EU General Data Protection Regulation 2018 and the University of Birmingham Research Guidelines.

WHAT WILL HAPPEN TO THE RESULTS OF THE STUDY?

All data for presentation will be anonymised, that means your identity will not be revealed in any way. The findings from this study will be presented, or shared with other researchers in the form of presentations and scientific papers as appropriate.

DOES THE STUDY FOLLOW ETHICS PROCEDURES?

This study underwent the ethical review processes of the University of Birmingham and received official approval from the University Ethics Committee.

WHO IS ORGANISING AND FUNDING THE RESEARCH?

The study has been designed and organised by Ahmed Alalawi and is overseen by Professor Deborah Falla, Chair in Rehabilitation Science and Physiotherapy

For further information please contact Ahmed Alalawi

Ahmed Alalawi Centre of Precision Rehabilitation for Spinal Pain School of Sports, Exercise and Rehabilitation Sciences University of Birmingham B15 2TT	

Thank you for taking the time to read this and considering taking part in the study!

Appendix 26: Participant information sheet for people with chronic neck pain

UNIVERSITY OF BIRMINGHAM | CENTRE OF PRECISION REHABILITATION FOR SPINAL PAIN

Neuromuscular adaptations in people with recurrent neck pain during a period of remission

We are looking for volunteers to take part in a research study. Before you decide whether you would like to take part, it is important that you know what the study is about and what it would involve for you. This is explained below; please read the information carefully.

WHAT IS THE STUDY ABOUT?

Research has shown that movement and muscle activity is altered in people with chronic neck pain. What is not known, is whether neck muscle activity and coordination in people with recurrent neck pain (painful episodes followed by asymptomatic periods) are altered and if ongoing alterations in muscle function could negatively influence the ongoing nature of pain. Therefore, the main purpose of the study is to investigate neck muscle activity and movement in people with recurrent neck pain, then data will be compared with healthy volunteers and people with chronic neck pain with current symptoms.

CAN I PARTICIPATE?

You can participate if you meet the following criteria:

- Have had a prior whiplash injury;
- Have chronic neck pain for at least 3 months;
- Age between 18 and 65 years;

You must also ***not*** fall in any of the categories below:

previous spinal or shoulder surgery, neck or shoulder injury that resulted in a fracture, current neuropathies/radiculopathies, neurological deficits, rheumatic condition, pregnancy; participation in a neck shoulder exercise program in the past 3 months.

We will ask you to complete a brief screening assessment to ensure you are eligible to participate. This will be performed by an experienced researcher and will include questions about your general health.

WHAT WILL I HAVE TO DO IF I PARTICIPATE?

We will ask that you to attend one data collection session, taking approximately 2 hours; this session can be organised at a time that will suit you. During this session, we will analyse your neck movements (flexion, extension, and rotation) and the activity of your cervical muscles by surface electromyography. At first, in order to analyse movement, fitted elastic straps will be used to place inertial measurement units on your forehead and over your back. An inertial measurement unit is a wearable sensor similar to a little box (dimensions of approximately 5x4x2 cm). Then, during the second part of the experiment, we will place surface electrodes (like ECG electrodes) on your skin to record the activity of your neck muscles and we will ask you to perform static contractions. We will ask you to bring a top for this session in order to perform movements in a comfortable way. The experiment will take place in the CPR Spine labs.

HOW MUCH TIME WILL I HAVE TO SPEND IN TOTAL?

The questionnaires will require approximately 20-30 minutes. Data collection in the lab will last approximately 2 hours. Questionnaires will cover the following topics: neck pain and disability, physical activity, fear of movement and health related quality of life.

ARE THERE ANY BENEFITS FOR ME IF I TAKE PART?

You will gain a better understanding of your neck movement and how your neck muscles activate and how these features may be linked to pain that you are experiencing.

ARE THERE ANY RISKS FOR ME IF I TAKE PART?
The risks are low, as all procedures are carried out by experienced professionals and you will be thoroughly screened to ensure that it is safe for you to take part. All tests performed are non-invasive. You may experience discomfort, or dizziness during repeated neck movements. You may also feel discomfort and fatigue during the muscle contractions. If, however you feel any discomfort or pain during any aspect of the study, then you will be free to stop and should you wish, you can withdraw from the study.

ARE THERE ANY COST OR REIMBURSEMENTS FOR ME?
There is no cost for this study, but you will be compensated £15 for attending the full laboratory session. If you choose to withdraw, you will be offered partial compensation which is determined by the amount of time the you were was present in the Lab before withdrawal.

DO I HAVE TO TAKE PART?
No, participation is entirely voluntary. If you decide to take part but you change your mind, you can withdraw from the study at any point and up to two weeks following completion of data collection in the laboratory without having to give a reason.

WILL MY DATA BE KEPT CONFIDENTIAL?
All information collected on you will be kept strictly confidential. The consent form containing your allocated ID will never be present in electronic form, will be securely stored within CPR Spine and only available to the researchers. All data will be stored for 10 years managed in accordance with the EU General Data Protection Regulation 2018 and the University of Birmingham Research Guidelines.

WHAT WILL HAPPEN TO THE RESULTS OF THE STUDY?
All data for presentation will be anonymised, that means your identity will not be revealed in any way. The findings from this study will be presented, or shared with other researchers in the form of presentations and scientific papers as appropriate.

DOES THE STUDY FOLLOW ETHICS PROCEDURES?
This study underwent the ethical review processes of the University of Birmingham and received official approval from the University Ethics Committee.

WHO IS ORGANISING AND FUNDING THE RESEARCH?
The study has been designed and organised by Ahmed Alalawi and is overseen by Professor Deborah Falla, Chair in Rehabilitation Science and Physiotherapy [redacted]

For further information please contact Ahmed Alalawi

Ahmed Alalawi Centre of Precision Rehabilitation for Spinal Pain School of Sports, Exercise and Rehabilitation Sciences University of Birmingham B15 2TT	[redacted]

Thank you for taking the time to read this and considering taking part in the study!

Appendix 27: Initial recruitment poster for both groups with neck pain

UNIVERSITY OF BIRMINGHAM | CENTRE OF PRECISION REHABILITATION FOR SPINAL PAIN

Neck pain after a car accident?

Purpose: To investigate neck movement and muscle activity in **people who have had a whiplash injury**

We are looking for people with a **recurrent neck pain** who:

- Have had a **prior whiplash injury after a car accident;**
- Have had **2 or more neck pain episodes** over the last year;
- Pain episodes lasted **24 hours or more**;
- **Pain-free** for at least **10 days;**
- Are aged between 18-65;

we are also looking for people with a **chronic neck pain** who:

- Have had a **prior whiplash injury after a car accident;**
- Have had Neck Pain for **more than 3 months;**
- Are aged between 18-65;

What do you need to do?

- This study will involve **one lab session** of approximately 2 hours.
- We will use sensors and electromyography to analyse your movement and muscular activity

You will be compensated £15 for your participation

For more information on how to take part, please contact Ahmed Alalawi at [redacted].

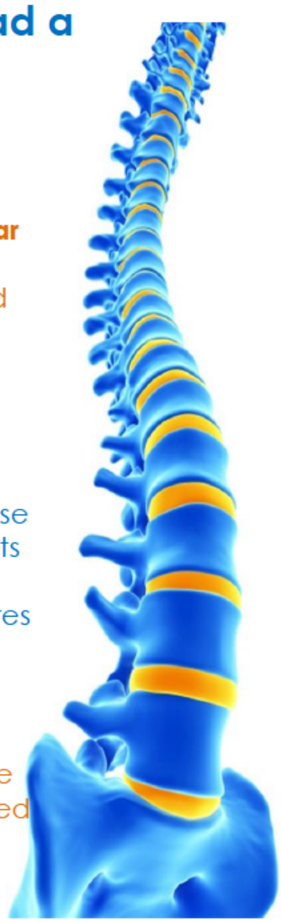
SCAN ME

Appendix 28: Modified (amendments 1) recruitment poster for people with recurrent neck pain (within UoB campus)

UNIVERSITY OF BIRMINGHAM | CENTRE OF PRECISION REHABILITATION FOR SPINAL PAIN

WHIPLASH ?

Purpose: To investigate neck movement and muscle activity in **people who have had a whiplash injury**



We are currently recruiting people who:

- Have had a **prior whiplash injury**
- Are aged between 18-65
- Have had **2 or more neck pain episodes over the last year**
- **Pain-free** over the last 10 days
- Your pain is not linked to fractures, and you have not had neck surgery

What do you need to do?

This study will involve one lab session of approximately 2 hours
We will use wearable sensors and electromyography to analyse your movement and muscular activity during neck movements and muscle contractions.
We will ask you to fill out an additional electronic questionnaires once a month over the course of 12 months

For completing this study, you will be compensated £15 for attending the laboratory session, £5 per monthly questionnaire completed and £20 extra if all 12 questionnaires are completed

£95 overall

For more information on how to take part, please contact

Appendix 29: Recruitment poster (amendments 1) for people with recurrent neck pain (Facebook post)

Hello

We are currently recruiting individuals who have had a whiplash injury. The study will involve one lab session and electronic questionnaires and you will be reimbursed for your time (£95 overall).

Please see the attached participant information sheet for more information.

Participants are Needed!

Hello

I am looking for people with history of recurrent neck pain or chronic neck pain initiated following a whiplash injury. The study will involve one lab session (2 hours) and you will be reimbursed for your time (£15).
Please see the inclusion criteria for each group:

1. Recurrent neck pain group:
   - Have had a prior whiplash injury;
   - Have had 2 or more neck pain episodes over the last year;
   - Pain episodes lasted 24 hours or more;
   - Pain-free for at least 10 days;

2. Chronic neck pain group:
   - Have had a prior whiplash injury;
   - Have had Neck Pain for more than 3 months;

If you are interested or have any questions, please massage me directly or contact me on

Please see the attached participant information sheet for more information.

Appendix 30: Recruitment poster (amendments 2) for people with recurrent neck pain (Facebook post)

Be part of our research about neck pain following a car accident (whiplash injury).

We will assess your neck and offer you £15, in exchange for 2 hours of your time at the University of Birmingham. Register your interest at the website:

Appendix 31: Recruitment poster (amendments 1) for people with recurrent neck pain (Local newspaper)

https://issuu.com/philby176/docs/hem-life-october-2019

Volunteers needed with recurrent neck pain following a whiplash injury

What will it involve?

- You will be invited to visit our research facility at the University of Birmingham on one occasion which will lasts about 2 hours.
- We will use special sensors to analyse your movement and muscular activity during neck movements and muscle contractions.
- We will ask you to fill out an additional electronic questionnaire once a month over the course of 12 months.

Who can participate?

- Have had a prior whiplash injury
- Are aged between 18-65
- Have had 2 or more neck pain episodes over the last year
- Pain-free over the last 10 days
- Your pain is not linked to fractures, and you have not had neck surgery.

What is the purpose?

We would like to investigate neck movement and muscle activity in people who have had a whiplash injury. Please read on for more detailed information.

UNIVERSITY OF BIRMINGHAM | CENTRE OF PRECISION REHABILITATION FOR SPINAL PAIN

If you are interested or have any further questions, please contact
Ahmed Alalawi: or
Professor Deborah Falla:
You will be reimbursed for your time up to £95.

Have you had a whiplash injury?

We are looking for volunteers to take part in a research study focused on neck pain related to a whiplash injury which will be conducted at the Centre of Precision Rehabilitation for Spinal Pain (CPR Spine) located at the University of Birmingham. CPR Spine is the first centre in the United Kingdom dedicated specifically to spinal pain research and consists of a multi-disciplinary team with a common aim of identifying patient-specific interventions for people with spinal pain.

What is the study about?

Research has shown that movement and muscle activity are altered in people with neck pain following a whiplash injury. What is not known, is whether changes in neck muscle activity persist when people have pain relief, and whether these persistent changes in muscle activity can contribute to future episodes of neck pain. Therefore, the main purpose of the study is to investigate neck muscle activity in people who have had a whiplash injury but currently are not experiencing neck pain. This data will be compared with pain-free volunteers and people with neck pain following a whiplash injury with current symptoms.

Am I eligible to participate?

We are seeking to recruit people who are aged between 18 and 65 years and have had a prior whiplash injury but have been free of neck pain over the last 10 days.

How will my participation help?

Your participation in this research is important as it could help us to understand and identify features which cause repeated episodes of neck pain. This will then help us to develop new examination and management approaches for people suffering with pain following a whiplash injury.

What will I need to do if I participate?

If you participate, you will obtain a thorough examination of your neck movement and muscle activity. The measurements will be conducted in a laboratory at the University of Birmingham during a single session of approximately 2 hours duration. You will then be asked to complete an electronic questionnaire to describe your neck pain, once a month for up to 12 months.

Are there any costs or reimbursements for my time?

There is no cost for you to participate in this study. You will be compensated £15 for attending the full laboratory session. Moreover, you will receive an additional £5 per monthly questionnaire completed for an additional £60 if all 12 questionnaires are completed. Finally, if you are able to complete the entire set of 12 questionnaires you will receive a further £20 to acknowledge your involvement in the entire study. Thus, a maximum of £95 will be provided upon full completion of the study.

For further information please contact

Appendix 32: Consent form for people with recurrent neck pain

Consent Form

Study ID: Participant identification Number:

Neuromuscular adaptations in people with recurrent neck pain during a period of remission

This information is being collected as part of a research project concerned with the investigation of neuromuscular functions in people with recurrent and chronic neck pain by the Centre of Precision Rehabilitation of Spinal Pain within the School of Sport, Exercise and Rehabilitation Sciences at the University of Birmingham. The information which you supply and that which may be collected as part of the research project will be entered into a filing system or database and will only be accessed by authorised personnel involved in the project. The information will be retained by the University of Birmingham and will only be used for the purpose of research and statistical and audit purposes. By supplying this information you are consenting to the University storing your information for the purposes stated above. The information will be processed by the University of Birmingham in accordance with the provisions of the EU General Data Protection Regulation 2018. No identifiable personal data will be published.

Please initial each box if you agree with the statement and sign the form

	I confirm that I have read and understand the 'participant information form' for this study. I have had the opportunity to ask questions if necessary and have had these answered satisfactorily.
	I understand that my participation is voluntary and that I am free to withdraw at any time without giving any reason as I will have the right to withdraw my data from the study up to two weeks following completion of the last questionnaire. If I withdraw my data will be removed from the study and will be destroyed. I will be free to withdraw at any time during the experimental session.
	I understand that my personal data will be processed for the purposes detailed above, in accordance with the EU General Data Protection Regulation 2018.
	I agree that my information may be used in research and presented and/or published in the research literature anonymously.
	Based upon the above, I agree to take part in this study.

Name of participant……………………… Date…………… Signature………………..

Name of researcher/ individual obtaining consent………………………… Date…………… Signature………………..

<u>Contact details of participant</u>

Contact number: Email address:

Appendix 33: Consent form for people with chronic neck pain and healthy participants

Consent Form

Study ID:

Neuromuscular adaptations in people with recurrent neck pain during a period of remission

This information is being collected as part of a research project concerned with the investigation of neuromuscular functions in people with recurrent and chronic neck pain by the Centre of Precision Rehabilitation of Spinal Pain within the School of Sport, Exercise and Rehabilitation Sciences at the University of Birmingham. The information which you supply and that which may be collected as part of the research project will be entered into a filing system or database and will only be accessed by authorised personnel involved in the project. The information will be retained by the University of Birmingham and will only be used for the purpose of research and statistical and audit purposes. By supplying this information you are consenting to the University storing your information for the purposes stated above. The information will be processed by the University of Birmingham in accordance with the provisions of the EU General Data Protection Regulation 2018. No identifiable personal data will be published.

Please initial each box if you agree with the statement and sign the form

	I confirm that I have read and understand the 'participant information form' for this study. I have had the opportunity to ask questions if necessary and have had these answered satisfactorily.
	I understand that my participation is voluntary and that I am free to withdraw at any time without giving any reason as I will have the right to withdraw my data from the study up to two weeks following completion of data collection. If I withdraw my data will be removed from the study and will be destroyed. I will be free to withdraw at any time during the experimental session.
	I understand that my personal data will be processed for the purposes detailed above, in accordance with the EU General Data Protection Regulation 2018.
	I agree that my information may be used in research and presented and/or published in the research literature anonymously.
	Based upon the above, I agree to take part in this study.

Name of participant……………………… Date………….. Signature………………..

Name of researcher/ individual obtaining consent………………………… Date………….. Signature………………..

<u>Contact details of participant</u>

Contact number: Email address:

Appendix 34: Eligibility criteria and baseline self-reported outcome measures

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Eligibility Criteria

P ease comp ete the survey be ow.

Thank you!

	P ease, wr te your Record ID (ask the researcher)	______________
	P ease, se ect the date of comp et on	______________
1	What s your age?	______________
2	What s your gender?	◯ Ma e ◯ Fema e
	What s your we ght (kg)?	______________
	What s your he ght (m)?	______________
3	Do you suffer from neck pa n?	◯ No, I am asymptomat c ◯ Yes, I suffer from recurrent neck pa n ◯ Yes, I suffer from chron c neck pa n
3.1	In the past, have you ever suffered from neck or shou der pa n that requ red treatments from a hea thcare profess ona ?	◯ Yes ◯ No
3.1	How d d your neck pa n started?	◯ Id opath c (unknown or g n) ◯ Wh p ash njury ◯ Other
3.1.1	P ease, spec fy the or g n	______________
3.2	Over the ast year, how many ep sodes of neck pa n have you had?	______________
3.3	Were your neck pa n ep sodes separated by 30 or more days of rem ss on?	◯ Yes ◯ No
3.4	Over the ast month, have you had neck pa n ep sodes?	◯ Yes ◯ No
3.5	P ease, se ect the number on the s der that best represents the ntens ty of your pa n DURING a neck pa n EPISODE	No pa n — Worst pa n poss b e *(Place a mark on the scale above)*
	P ease, se ect the number on the s der that best represents the ntens ty of your current neck pa n (NOW)	No pa n (0) — Worst pa n poss b e (100) *(Place a mark on the scale above)*

3.2	How many months have you been suffer ng from pers stent neck pa n?	______________________
3.3	P ease, se ect the number on the s der that best represents the ntens ty of your current neck pa n (NOW)	No pa n — Worst pa n poss b e *(Place a mark on the scale above)*
4	Have you ever had sp na or shou der surgery?	◯ Yes ◯ No
5	Have you ever had neck or shou der fractures?	◯ Yes ◯ No
6	Do you suffer from neuropath es/rad cu opath es or neuro og ca def c ts?	◯ Yes ◯ No
7	Do you suffer from rheumat c d sorders?	◯ Yes ◯ No
8	Over the ast 3 months, have you part c pated n a neck or shou der exerc se program?	◯ Yes ◯ No
9	Are you pregnant?	◯ Yes ◯ No
	P ease se ect the reg on(s) where you usua y fee neck pa n	______________________

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Neck Disability Index

P ease comp ete the survey be ow.

Thank you!

This questionnaire has been designed to give us information as to how your back or leg pain is affecting your ability to manage in everyday life. Please answer by checking ONE box in each section for the statement which best applies to you.

We realise you may consider that two or more statements in any one section apply but please just shade out the spot that indicates the statement which most clearly describes your problem.

1) Sect on 1 - Pa n Intens ty

- ◯ I have no neck pa n at the moment
- ◯ The neck pa n s very m d at the moment
- ◯ The neck pa n s moderate at the moment
- ◯ The neck pa n s fa r y severe at the moment
- ◯ The neck pa n s very severe at the moment
- ◯ The neck pa n s the worst mag nab e at the moment

2) Sect on 2 - Persona care

- ◯ I can ook after myse f norma y w thout caus ng extra neck pa n
- ◯ I can ook after myse f norma y but causes extra neck pa n
- ◯ It s pa nfu to ook after myse f and I am s ow and carefu
- ◯ I need he p some he p but manage most of my persona care
- ◯ I need he p every day n most aspects of se f-care
- ◯ I do not get dressed, I wash w th d ff cu ty and stay n bed

3) Sect on 3 - L ft ng

- ◯ I can ft heavy we ghts w thout extra neck pa n
- ◯ I can ft heavy we ghts but t g ves extra neck pa n
- ◯ Neck pa n prevents me from ft ng heavy we ghts off the f oor, but I can manage f they are conven ent y p aced eg. on a tab e
- ◯ Neck pa n prevents me from ft ng heavy we ghts,but I can manage ght to med um we ghts f they are conven ent y pos t oned
- ◯ I can ft very ght we ghts
- ◯ I cannot ft or carry anyth ng at a

4) Sect on 4 - Read ng

- ◯ I can read as much as I want w th no neck pa n
- ◯ I can read as much as I want w th s ght neck pa n
- ◯ I can read as much as I want w th moderate neck pa n
- ◯ I can't read as much as I want because of moderate neck pa n
- ◯ I can't read as much as I want because of severe neck pa n
- ◯ I can't read at a

5) Sect on 5 - Headaches

◯ I have no headaches at a
◯ I have s ght headaches that come nfrequent y
◯ I have moderate headaches that come nfrequent y
◯ I have moderate headaches that come frequent y
◯ I have severe headaches that come frequent y
◯ I have headaches a most a the t me

6) Sect on 6 - Concentrat on

◯ I can concentrate fu y w thout d ff cu ty
◯ I can concentrate fu y w th s ght d ff cu ty
◯ I have a fa r degree of d ff cu ty concentrat ng
◯ I have a ot of d ff cu ty concentrat ng
◯ I have a great dea of d ff cu ty concentrat ng
◯ I can't concentrate at a

7) Sect on 7 - Work

◯ I can do as much work as I want
◯ I can do my usua work, but no more
◯ I can do most of my usua work, but no more
◯ I can't do my usua work
◯ I can hard y do any work at a
◯ I can't do any work at a

8) Sect on 8 - Dr v ng

◯ I can dr ve my car w thout neck pa n
◯ I can dr ve my car w th on y s ght neck pa n
◯ I can dr ve as ong as I want w th moderate neck pa n
◯ I can dr ve as ong as I want because of moderate neck pa n
◯ I can hard y dr ve at a because of severe neck pa n
◯ I can't dr ve my var at a because of neck pa n

9) Sect on 9 - S eep ng

◯ I have no troub e s eep ng
◯ My s eep s s ght y d sturbed for ess than 1 hour
◯ My s eep s m d y d sturbed for up to 1-2 hours
◯ My s eep s moderate y d sturbed for up to 2-3 hours
◯ My s eep s great y d sturbed for up to 3-5 hours
◯ My s eep s comp ete y d sturbed for up to 5-7 hours

10) Sect on 10 - Recreat on

◯ I am ab e to engage n a my recreat ona act v t es w th no neck pa n at a
◯ I am ab e to engage n a my recreat ona act v t es w th some neck pa n
◯ I am ab e to engage n most, but not a my recreat ona act v t es because of pa n n my neck
◯ I am ab e to engage n a few of my recreat ona act v t es because of pa n n my neck
◯ I can hard y do recreat ona act v t es due to neck pa n
◯ I can't do any recreat ona act v t es due to neck pa n

11) Score

____

Tampa Scale For Kinesiophobia

P ease comp ete the survey be ow.

Thank you!

Tampa Scale for Kinesiophobia (Miller, Kori and Todd 1991)

		strong y d sagree	d sagree	agree	strong y agree
1)	I'm afra d that I m ght njury myse f f I exerc se	○	○	○	○
2)	If I were to try to overcome t, my pa n wou d ncrease	○	○	○	○
3)	My body s te ng me I have someth ng dangerous y wrong	○	○	○	○
4)	My pa n wou d probab y be re eved f I were to exerc se	○	○	○	○
5)	Peop e aren't ta k ng my med ca cond t on ser ous y enough	○	○	○	○
6)	My acc dent has put my body at r sk for the rest of my fe	○	○	○	○
7)	Pa n a ways means I have njured my body	○	○	○	○
8)	Just because someth ng aggravates my pa n does not mean t s dangerous	○	○	○	○
9)	I am afra d that I m ght njure myse f acc denta y	○	○	○	○
10)	S mp y be ng carefu that I do not make any unnecessary movements s the safest th ng I can do to prevent my pa n from worsen ng	○	○	○	○
11)	I wou dn't have th s much pa n f there weren't someth ng potent a y dangerous go ng on n my body	○	○	○	○
12)	A though my cond t on s pa nfu , I wou d be better off f I were phys ca y act ve	○	○	○	○
13)	Pa n ets me know when to stop exerc s ng so that I don't njure myse f	○	○	○	○
14)					

	It's rea y not safe for a person w th a cond t on ke m ne to be phys ca y act ve	○	○	○	○
15)	I can't do a the th ngs norma peop e do because t's too easy for me to get njured	○	○	○	○
16)	Even though someth ng s caus ng me a ot of pa n, I don't th nk t's actua y dangerous	○	○	○	○
17)	No one shou d have to exerc se when he/she s n pa n	○	○	○	○

18) Tota Score ______________________

Eq5d

P ease comp ete the survey be ow.

Thank you!

---

1) MOBILITY

◯ I have no prob ems n wa k ng about
◯ I have s ght prob ems n wa k ng about
◯ I have moderate prob ems n wa k ng about
◯ I have severe prob ems n wa k ng about
◯ I am unab e to wa k about

---

2) SELF-CARE

◯ I have no prob ems wash ng or dress ng myse f
◯ I have s ght prob ems wash ng or dress ng myse f
◯ I have moderate prob ems wash ng or dress ng myse f
◯ I have severe prob ems wash ng or dress ng myse f
◯ I am unab e to wash or dress myse f

---

3) USUAL ACTIVITIES (e.g. work, study, housework, fam y or e sure act v t es)

◯ I have no prob ems do ng my usua act v t es
◯ I have s ght prob ems do ng my usua act v t es
◯ I have moderate prob ems do ng my usua act v t es
◯ I have severe prob ems do ng my usua act v t es
◯ I am unab e to do my ususa act v t es

---

4) PAIN/DISCOMFORT

◯ I have no pa n or d scomfort
◯ I have s ght pa n or d scomfort
◯ I have moderate pa n or d scomfort
◯ I have severe pa n or d scomfort
◯ I have extreme pa n and d scomfort

---

5) ANXIETY / DEPRESSION

◯ I am not anx ous or depressed
◯ I am s ght y anx ous or depressed
◯ I am moderate y anx ous or depressed
◯ I am severe y anx ous or depressed
◯ I am extreme y anx ous or depressed

---

6) We wou d   ke to know how good or bad your hea th s TODAY.
Th s sca e s numbered from 0 to 100.

100 means the best hea th you can mag ne.
0 means the worst hea th you can mag ne.
Move the s der on the sca e to nd cate how your hea th s TODAY

0 - The worst pa n you can mag ne | 100 - The best hea th you can mag ne

(Place a mark on the scale above)

Appendix 35: Outcome measures for the longitudinal analysis

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Page 1

Followup Questionnaire

P ease comp ete the survey be ow.

Thank you!

Date of comp et on: ______________________________

---

1 Over the past month, how many days have you suffered from neck pa n? ______________________________

1.1 Over the past month, do you know f a spec f c cause tr ggered your neck pa n (p ease se ect one or more opt ons)?

- ☐ Sudden movement
- ☐ Trauma
- ☐ Work ng posture
- ☐ Le sure / Sport act v t es
- ☐ Neck pos t on dur ng s eep
- ☐ I don't know
- ☐ Other

1.2 You have t cked OTHER, p ease spec fy the cause/s

____

---

2 Over the past month, how wou d you rate your average neck pa n?

No pa n (0) — Worst pa n poss b e (100)

(Place a mark on the scale above)

---

3 Over the past month, how wou d you rate your neck pa n eve at ts worst?

No pa n (0) — Worst pa n poss b e (100)

(Place a mark on the scale above)

---

4 Over the past month, how many days have you been on s ck eave for your neck pa n? ______________________________

---

5 Over the past month, how much has your neck pa n nterfered w th your work?

No nterference (0) — Unab e to work (100)

(Place a mark on the scale above)

---

6 Over the past month, how much has your neck pa n nterfered w th your da y act v t es (housework, wash ng, dress ng, ft ng, read ng, dr v ng)?

No nterference (0) — Unab e to carry out act v ty (100)

(Place a mark on the scale above)

---

7 Over the past month, how much has your neck pa n nterfered w th your ab ty to take part n recreat ona , soc a , and fam y act v t es?

No nterference (0) — Unab e to carry out act v ty (100)

(Place a mark on the scale above)

8 Over the past month, how much have you been ab e to contro (reduce/he p) your neck pa n on your own?

No contro whatsover (0) — Comp ete y contro of t (100)

(Place a mark on the scale above)

9 Over the past month, have you sought med ca consu tat on or treatment (phys c an, phys ca therap st, psycho og st, ch ropractor, comp ementary care) for your neck pa n?

◯ Yes ◯ No

9.1 P ease, report the number of ntervent ons:

____

9.2 P ease, nd cate the type of ntervent ons (se ect one or more opt ons):

☐ Phys c an
☐ Phys ca Therap st
☐ Massage Therap st
☐ Psycho og st
☐ Ch ropractor
☐ Osteopath
☐ Other

9.3 You have t cked OTHER, p ease spec fy the type of ntervent on/s

____

Over the past month, d d you perform exerc ses for your neck d sorder?

◯ Yes ◯ No

P ease, prov de more nformat on about the exerc ses that you performed

____

10 Over the past month, how many days have you taken med cat on to contro your neck pa n (p ease report on y one number)?

____

10.1 What k nd of pa n med cat on?

☐ Paracetamo
☐ NSAIDs
☐ Op o d pa nk ers
☐ Musc e re axants
☐ Other

10.2 You have t cked OTHER, p ease spec fy the k nd of med cat on/s

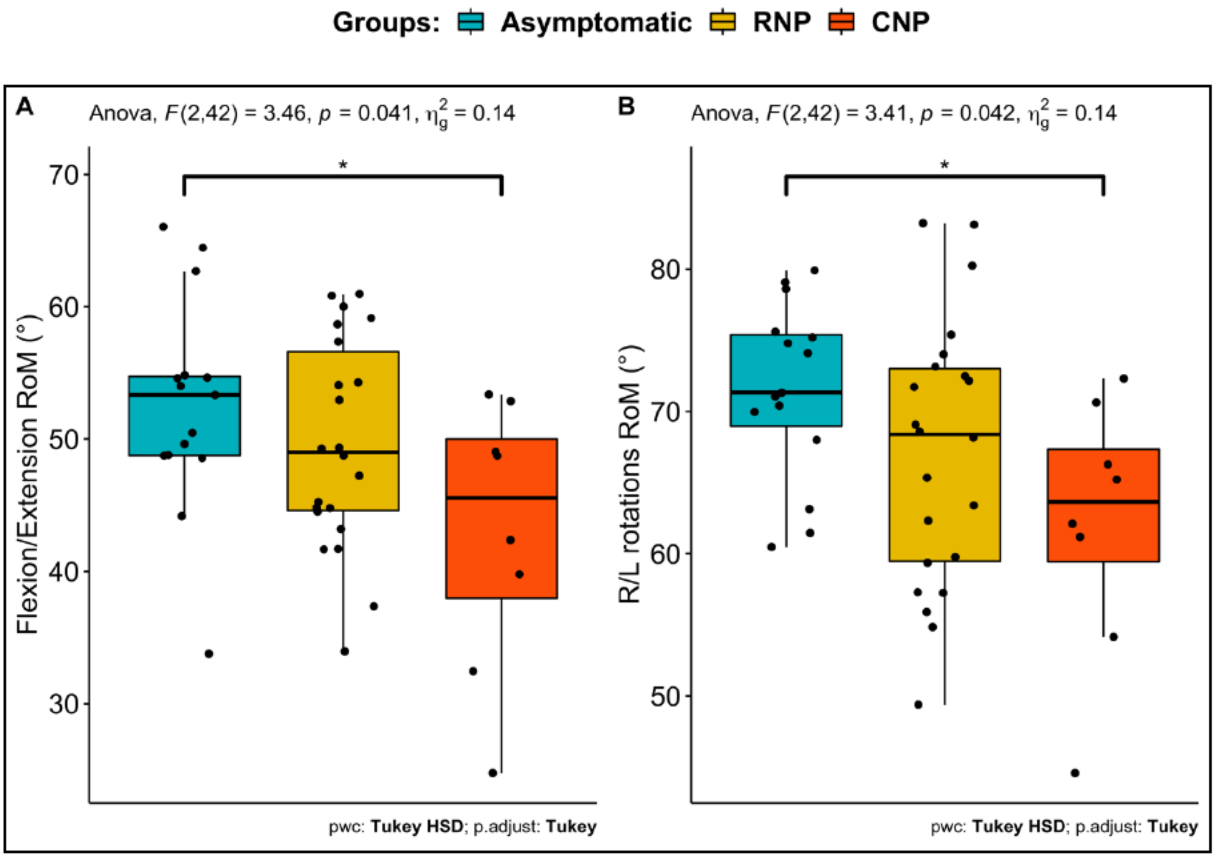
____

11 Over the past month, how much has your neck pa n d sturbed your s eep qua ty?

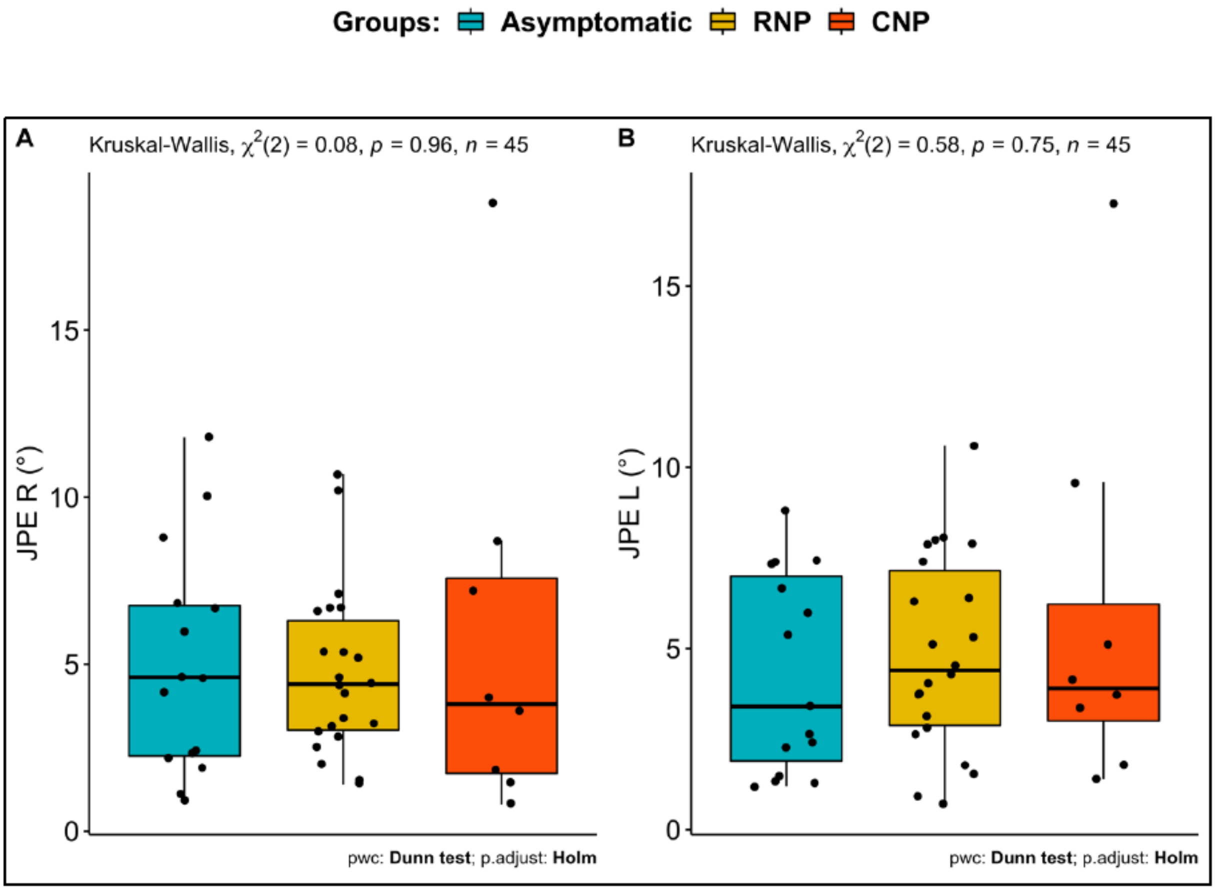
Not at a (0) — Extreme y (100)

(Place a mark on the scale above)

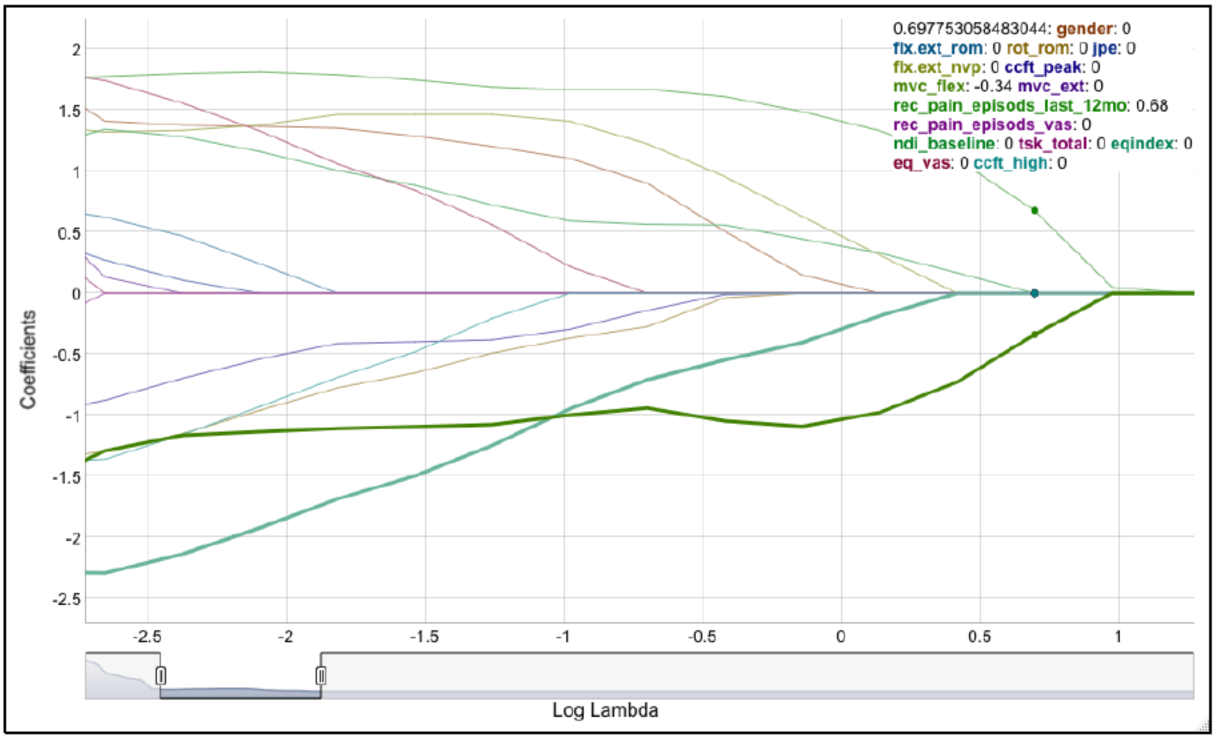
Appendix 36: Box plots for cervical kinematics and proprioception



Appendix 37: Box plots for joint position error



Appendix 38: Graph for coefficients paths of LASSO regression (outcome: NDI at six months)



Appendix 39: Graph for coefficients paths of LASSO regression (outcome: number of days with pain over the 12-month period)