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Introduction

Neck pain is a highly prevalent issue that most individuals can expect to experience at least once within their lifetime.[1] In the United States alone, an estimated 15.7% of the population reported neck pain in 2015.[2] While acute neck pain may resolve on its own, cervical pain may develop into a chronic issue that can result in economic burden, negatively impact quality of life, and cause social hardship.[1] The treatment strategies utilized by physical therapist to treat neck pain are widely variable and lack clinical evidence. As such, identifying cost-effective treatment options that result in good outcomes has been identified as a priority for physical therapists.[3]

In order to address this issue, a strategy that has been proposed involves basing treatment decisions on prognostic factors that can stratify patients into two groups; those at high risk for developing persistent neck pain and disability and those that are likely to recover regardless of the intensity of treatment received.[3] Identifying the presence or absence of various prognostic variables during the initial examination can aid clinicians make more accurate prognosis and guide treatment decisions, which may lead to a more cost-effective and successful plan of care. A number of studies have identified variables that predict outcome in patients seeking treatment for neck pain. These include various physical, sociodemographic, clinical, and psychological variables.

Prognostic Factors

Age

McLean et al.[4] conducted a systematic review of nine prospective cohort studies identifying prognostic factors of non-specific neck pain. They conclude that there is strong evidence linking "older age" to unfavorable outcomes in regards to both resolution of symptoms and neck-related disability in subjects with non-specific neck pain. Generally speaking, old age in these studies was defined as over 40 years of age[5–8], with one study not defining what they considered older age to be.[9] Contrary to these findings, Cecchi et al.[10] conclude that age is not

predictive of improvement after physical therapy treatment at discharge nor at one-year follow up in their cohort of subjects with chronic, non-specific neck pain and disability. The subjects in Cecchi's[10] study, however, include mostly elderly and middle aged women. Most of the subjects in this study would have been categorized as "older age", which explains why Cecchi et al.[10] conclude that age is not a good predictor of treatment outcome.

Duration of Symptoms

McLean et al.[4] also identify two high quality studies that concluded longer duration of neck pain is strongly prognostic of unfavorable outcome in terms of neck-related disability and symptom resolution.[4] Longer duration of symptoms was defined as 13 weeks (Hoving, 2004)[8] and 24 weeks (Bot, 2005)[11]. Cecchi et al.[10], however, found that time from onset of symptoms was not a good predictor of treatment outcome. Cecchi et al.[10] chose not to use an inception cohort in their study and therefore cannot exclude that their chronic subjects were not seeking treatment for acute symptom exacerbation, which could explain their findings regarding the duration of symptoms as a prognostic factor.

Baseline Pain and Disability

Few studies have linked initial neck disability to outcome. According to De Pauw et al.[12], higher neck disability index (NDI) scores at baseline are related to poorer outcomes. Likewise, patients scoring a NDI score of less than 18/50 at baseline may be more likely to perceive improvement after treatment.[13] In regards to whiplash associated injuries, a NDI score greater than 14.5/50 is related to poor patient outcomes.[14] In another study, Hill et al.[5] measured baseline neck pain and disability using The Northwick Park Neck Pain Questionnaire (NPQ) in their cohort of subjects with neck pain. They report that high baseline NPQ scores were a significant predictor of poor outcome as measured by perceived global change and achieving the minimum clinically important difference (MCID) on the NPQ.[5] A systematic review completed by Walton et al.[15] determine that high neck pain intensity, as measured by the VAS and NPRS, is highly prognostic for poor outcome in patients with whiplash injuries. Walton[15]

does state that there is limited evidence, however, for initial pain intensity in other causes of neck pain.[15] Likewise, McLean et al.[4] concluded in their review of the literature that there is inconclusive evidence for the predictive power of baseline disability and neck pain for subjects with non-specific neck pain, which is in agreement with the findings of Cecchi et al.[10]

Radicular Symptoms

Little evidence exists regarding the significance of radicular symptoms has on patient outcomes. A systematic review by Borghouts et al.[16] claims that there is weak evidence indicating radicular symptoms are not associated with poor outcomes. The review, however, relied almost entirely on the findings from observational and case-control studies. In regards to whiplash associated disorders, Walton et al.[15] determine that there is possible prognostic value of patient-reported radicular symptoms at inception and poor outcome, but this finding is inconsistent across systematic reviews.

Medications

Only one study has found a correlation between medication intake and patient outcome. In a study by Cecchi et al.[10], subjects reporting the use of neck pain medication at baseline had poor outcomes immediately after discharge from a six-session program and at 1-year follow up. According to these authors, this is a novel finding that has not been reported in other studies. The type of pain medication used by subjects was not identified.

Widespread Pain

Only one study has examined the prognostic value of widespread pain in patient outcome. Atherton et al.[17] found that patients who reported widespread pain in the month prior to incurring whiplash injury were more likely to have poor outcomes. For non-specific neck pain, McLean et al.[4] determine there is strong evidence supporting a history of back, knee or hip pain at baseline to be independently prognostic of unfavorable outcome with regards to symptoms. In other words, having other musculoskeletal impairments at baseline could lead to poor outcomes in patients experiencing neck pain.

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Other Prognostic Factors

There are many other prognostic factors that have been found to be predictive of patient outcomes. In regards to non-specific neck pain, the systematic review conducted by Mclean et al.[4] found strong evidence for a history of neck problems to be predictive of unfavorable outcome. Croft et al.[18] and Saavedra-Hernández et al.[19] similarly determine a history of neck pain to be a significant predictive factor. Mclean et al.[4] also identify other prognostic factors that have limited evidence supporting their utility, meaning only one high quality study determined the predictive value of the prognostic factor. These factors include presence of headaches, persistent neck pain, patient reports of numbness in the hands, and physical trauma. History of low back pain has also been identified as prognostic factor (Croft, 2001)[18], as has the presence of comorbid back pain (Hill, 2007)[5].

Some studies have begun to examine psychological and sociodemographic prognostic factors in patients with neck pain. One study included in the systematic review by Mclean et al[4] found limited evidence for high levels of worrying as a prognostic factor. In regards to sociodemographic factors, limited evidence has been found supporting female gender, unemployment, little influence on work life, high job demands, repetitive work, lower level of perceived health, low quality of life scores, and less vitality as prognostic factors.[4] Michaelson et al.[11] found a low need to be social and be helped, along with high optimistic attitudes, predicted good outcomes in patients receiving multimodal treatment for chronic neck pain. Landers et al.[20] found that scores on the Fear-Avoidance Belief Questionnaire (FABQ) are a good tool to identify patients who are at risk for prolonged neck disability. Another study completed by Hill et al.[5] further support the use of psychosocial factors in predicting the course of neck pain, including manual social class, catastrophizing, anxiety and depression, and low treatment expectations. Lastly, Croft et al.[18] found that number of children, poor self-assessed health, and poor psychological status were significant risk factors for developing neck pain. Studies supporting the use of psychological and sociodemographic variables as prognostic factors in patients with

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neck pain is a relatively new area of research. The evidence available to date supports the use of these factors, however, more high quality studies must be conducted to establish the validity of these findings.

In a systematic review on prognostic variables for WAD, Walton et al.[14] identify 12 significant prognostic variables that can predict prognosis. The variables not mentioned previously include less than postsecondary education, female sex, no seatbelt used, history of neck pain, headache at inception, neck pain at inception, catastrophizing, presence of low back pain, WAD grade 2 or 3 (versus 0 or 1), and WAD grade 3 (versus 2). Other systematic reviews regarding WAD have found mixed evidence for post-traumatic stress symptoms, catastrophizing, and cold hypersensitivity and hyperalgesia as risk factors for negative outcome in patients with whiplash syndrome.[15]

Psychometric Properties of NDI

The Neck Disability Index (NDI) is the most commonly used self-report measure for evaluating patient status in neck pain clinical research.[21–23] In 2008, the developer of the NDI, Howard Vernon, published a summary covering the 17-year history of the NDI.[24] The author states that the NDI has been used in approximately 300 publications, translated into 22 languages, and has been endorsed by many clinical guidelines, making it the most widely used and strongly validated instrument to assess self-rated disability in patients with neck pain.[24] The NDI was originally modeled after the Oswestry Low Back Pain Disability Questionnaire and assesses both subjective symptoms and activities of daily living.[24] The questionnaire consist of ten items that assess pain intensity, personal care, lifting, sleep, driving, sexual intercourse, headache, concentration, reading, and work.[24] The NDI is scored on a scale of 0 to 50, with higher scores indicating higher neck-related disability.[24]

Strengths of the NDI include is its ability to be used in different subpopulations and the fact that it has been validated using many measures of function, pain, and clinical signs and symptoms.[22] A systematic review in 2009 by MacDermid et al.[21] synthesized information from 37

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studies addressing the psychometric properties of the NDI. The authors concluded that there was strong to moderate evidence for a variety of psychometric properties supporting the use of the NDI in patients suffering from acute or chronic neck pain with musculoskeletal or neurogenic origin.

      Reliability There is appropriate evidence supporting the test-retest reliability of the NDI in both acute and chronic populations. Reliability coefficients of over 0.90 have been reported in several studies.[21] In contrast to these findings are the results of recent high quality studies reporting significantly lower test-retest reliability coefficients.[25,26] MacDermid et al.[21] suggest the variation of these findings were a result of random differences in samples, actual differences in clinical subpopulations, study processes, and definitions of "stable." In this case, stable refers to the unchanging nature of the condition. Some studies evaluating the test-retest reliability of the NDI did not separate patients experiencing acute and chronic neck pain in their statistical analysis. For those studies that did separate subjects based on acuity, test-retest reliability varied from an *r* of 0.73 – 0.93 for acute patients and 0.89 – 0.99 in subjects with chronic neck pain.[21]

      Few studies have presented the standard error of measurement (SEM) or the minimal detectable change (MDC) for the NDI. Cleveland et al.[25] reported the largest MDC of 10.2 points in their cohort of subjects with cervical radiculopathy. According to Vernon[24], however, the NDI was not specifically designed for patients with cervical radiculopathy and does not reflect the NDI in its usual use. Vos et al.[27] reported the lowest MDC of 1.66 in their study sample that included patients with recurrent neck pain who were considered to have a stable condition. Despite these wide ranges in MDC, most values average around 5/50, or 10%.[21] Vernon suggested that the MDC be 5 points based on his review of the literature and expert opinion.[24]

      Table 1 provides results from studies that have reported the SEM of the NDI. The SEM has ranged from a low of 3.0 to to a high of 8.4, depending on the study population (table 1).

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Study	Standard Error of Measurement
Cervical Radiculopathy	
Cleland et al, 2006[25]	4.4
Young et al, 2010[28]	5.7
Mechanical Neck Disorder	
Cleland et al, 2008[26]	8.4
Young et al, 2009[29]	4.3
Non-Specific Neck Pain	
Jorristsma et al, 2012[30]	3.0

Table 1. Standard Error of Mean of NDI

Validity The construct of disability from neck pain, as measured by the NDI, has shown strong convergent validity with other questionnaires such as the Patient-Specific Functional Scale, the Northwick Park Neck Pain Questionnaire, the Neck Pain and Disability Score, and the Disability Rating Index. The correlations between the NDI and these scales have been reported to be greater than 0.70.[21]

Responsiveness Five studies have reported on the minimally clinical important difference (MCID).[24] The MCID has ranged from a low of 3.5 to a high of 10. Stratford et al [31] found a MCID of 5 out of 50 points by comparing scores on the NDI with a physician-rated change scale. Cleland et al.[32] determined the MCID to be 10 points in a sample of subjects with cervical radiculopathy. Vernon attributed this large MCID to the refractory nature of cervical radiculopathy.[24] Pool et al.[33] found an MCID of 3.5 points by comparing NDI change scores and global perceived change using the area under the curve. Citing his expert opinion, Vernon[24] concluded that 3.5 is the most appropriate MCID for the NDI. In a cohort of subjects with mechanical neck pain, Young et al.[29] reported an MCID and MDC of 7.5 and 10 points, respectively. These authors concluded that because 7.5 points is within the bounds of measurement error found in their study (MCD = 10.2), a 10-point change should be used as the MCID.[29] Cleland et al.[26] found a similar MCID of 9.5 points in their cohort of subjects with mechanical neck pain.

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Statistical Models

Multinomial Logistic Regression Analyses

It is common for health science studies to attempt to determine what influence one or more variables has on a dependent variable.[34] When the dependent variable is a continuous numerical value, a linear (or higher order) regression analysis is an appropriate statistical model. If, however, the dependent variable is categorical in nature, a logistic regression analysis is a more appropriate statistical model. Examples of categorical variables may include imaging (yes/no), medications (yes/no), pain category (acute/chronic). The aim of a logistic regression analysis is to determine the best model for explaining a categorical variable (dependent variable) based on a series of independent variables.[34] When the dependent variable is dichotomous (0 or 1), a logistic regression analysis is applied. When the dependent variable has more than two categories, a multinomial logistic regression analysis is required.

An example given by Domínguez-Almendros et al.[34] attempts to relate the variable 'weight at birth of a newborn infant' (<2000g, 2000-3500g, and >3500g) to the independent variable 'smoking mother' (yes/no). For this example, the best fit of two logistic models would be determined. If the category >3500 g is used as a reference value, then one logistic model evaluates the risk of birthweight >3500g versus the category of <2000g in the case of a smoking or nonsmoking mother. The second logistic regression model compares the risk of birthweight >3500g versus the category 2000g – 3500g in the case of a smoking or nonsmoking mother. These two logistic regressions would cover the entire set of possible values for newborn birth weight.

When significant independent variables have been determined from a univariate analysis, these variables can then be included in a hierarchical multivariate multinomial regression analysis. The purpose of this analysis is to assess the association between multiple independent variables and outcomes. A multivariable analysis determines the unique contributions of various independent factors to a single outcome.[35] In the case of multivariate

multinomial regression, the contribution each independent variable has to the polychotomized outcomes can be assessed. Polychotomous variables are variables that can have more than two possible outcomes. For example, an individual being treated for neck pain could be categorized as a low, high, or a non-responder to treatment. A multivariate analysis is needed in order to control for confounding, which occurs when the association between an independent factor and an outcome is affected by the relationship of other independent variables.[35]

Cervical Clinical Prediction Rules

A prognostic clinical prediction rule (CPR) is a tool that quantifies the contributions of various patient characteristics to create a set of variables that can be used to predict a patient's prognosis.[36] Prognostic CPRs allow clinicians to estimate the probability that a patient will exhibit a change in pain or disability in the future and can therefore be used to educate individuals about their anticipated outcome as well as prioritize patients for treatment.[37] The development of CPRs involve three stages. In the first stage (derivation), statistical analyses are performed to determine the variables in a group of subjects that have the strongest positive predictive power.[38] In the second stage (validation), CPRs are tested by the prospective application in a new group of patients.[38] Validated CPRs may be used with a greater level of confidence then those in the derivation stage. In the final stage (impact analysis), the CPR is tested to determine if application of the rule results in changed clinician behavior and improved patient outcomes.[38] A CPR that succeeds in this final state can be used confidently by clinicians to improve patient outcomes.[38]

Kelly et al.[39] systematically reviewed CPRs pertaining to neck pain and found 19 studies (Table 2) that reported on the development of 15 prognostic CPRs relating to the conservative management of patients with neck pain. Thirteen of these studies included patients with acute whiplash injuries, five studies were related to non-traumatic neck pain, and one study evaluated subjects with cervical radiculopathy. A majority of these prognostic CPRs remain within the derivation stage and therefore are not recommended for routine clinical use.[39] Clinicians may

instead consider using the individual variables contained within these models to inform judgments on prognosis.[38] Four prognostic models have undergone preliminary investigations of validity and may be better suited for clinical use.[39] No prognostic CPRs have undergone the final stage with an impact analysis.

A large range of variables have been identified across the 15 prognostic CPR models. Psychological and social predictor variables are prominently featured in a number prognostic CPRs, indicating that assessment of these variables is important to determine prognosis and improve patient outcomes.[39] Many of the models evaluated in Kelly et al.'s[39] systematic review determined that initial score on the NDI is a predictor for future pain and disability outcomes.[17,40–43] As such, assessment of a patient's neck disability at baseline may be a useful adjunct to a clinician's clinical decision making process regarding prognosis and treatment selection. In contrast to the results of our current study, no studies have identified gender, use of imaging, or active versus passive treatment in their final prediction models.

A number of studies have progressed to the validation stage of CPR development[15,43–48], however these studies have been classified as undergoing "narrow validation." Narrow validation involves testing the CPR in a setting and population that is similar to the one in which the CPR was derived, which limits its generalizability to a broader population.[39] Three prognostic CPRs regarding subjects with acute whiplash disorder have undergone narrow validation and therefore, clinicians must use caution in application of these results.[43,45,47,49] Only one model has undergone broad validation (Schellingerhout, 2010[46]), meaning that the CPR has been validated in a wider spectrum of patients and settings. CPRs undergoing broad validation are preferred over narrow validation as they have been show to maintain their accuracy in a variety of patients and settings.[38] The CPR developed by Schellingerhout et al.[46] has modest predictive power with a positive predictive value of 51% and a positive likelihood ratio of 1.6. The moderate predictive ability of this CPR, however, is unlikely to cause a significant shift in pre- to post-test probability.[39] While the number prognostic CPRs related to

neck pain have significantly increased over recent years, many of these models must undergo

validation before they can be recommended for clinical use. However, clinicians may choose to

implement the four validated CPRs (table 2) or individual predictor variables contained within

these models to help inform patient prognosis and selection of treatment.[39]

Prognostic CPRs
Atherton et al. (2006)[17]
Carroll et al. (2006)[50]
Cleland et al. (2007)[51]
Dagfinrud et al. (2013)[44]
Gabel et al. (2008)[52]
Grooten et al. (2007)[53]
Hartling et al. (2002)[54]
Kasch et al. (2001)[55]
Kasch et al. (2008)[45]
*Kasch et al. (2011)[48]
*Kasch et al. (2013)[49]
Landers et al. (2008)[56]
Nederhand et al. (2004)[41]
*Radanov and Sturzenegger (1996)[47]
Ritchie et al. (2013)[42]
*Ritchie et al. (2015)[43]
*Schellingerhout et al. (2010)[46]
Vos et al. (2009)[57]
Williamson et al. (2015)[40]

Table 2. Neck related prognostic CPRs.
*CPRs that have undergone narrow or broad validation.

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References:

1.   Manchikanti L, Singh V, Datta S, Cohen SP, Hirsch JA, American Society of Interventional Pain Physicians. Comprehensive review of epidemiology, scope, and impact of spinal pain. *Pain Physician*. 12(4):E35-70. http://www.ncbi.nlm.nih.gov/pubmed/19668291. Accessed November 28, 2016.
2.   Center for Health Statistics N. Vital and Health Statistics Series 10, No. 235 (12/2007). 2006.
3.   Cook C, Rodeghero J, Cleland J, Mintken P. A Preliminary Risk Stratification Model for Individuals with Neck Pain. *Musculoskeletal Care*. March 2015. doi:10.1002/msc.1098.
4.   McLean SM, May S, Moffett JK, Sharp DM, Gardiner E. Prognostic factors for progressive non-specific neck pain: a systematic review. *Phys Ther Rev*. 2007;12(3):207-220. doi:10.1179/108331907X222967.
5.   Hill JC, Lewis M, Sim J, Hay EM, Dziedzic K. Predictors of poor outcome in patients with neck pain treated by physical therapy. *Clin J Pain*. 2007;23(8):683-690. doi:10.1097/AJP.0b013e3181468e67.
6.   Hill J, Lewis M, Papageorgiou AC, Dziedzic K, Croft P. Predicting persistent neck pain: a 1-year follow-up of a population cohort. *Spine (Phila Pa 1976)*. 2004;29(15):1648-1654. doi:10.1097/01.BRS.0000132307.06321.3C.
7.   Cassou B, Derriennic F, Monfort C, Norton J, Touranchet a. Chronic neck and shoulder pain, age, and working conditions: longitudinal results from a large random sample in France. *Occup Environ Med*. 2002;59(8):537-544. doi:10.1136/oem.59.8.537.
8.   Hoving JL, De Vet HCW, Twisk JWR, et al. Prognostic factors for neck pain in general practice. *Pain*. 2004;110(3):639-645. doi:10.1016/j.pain.2004.05.002.
9.   Bot SDM, van der Waal JM, Terwee CB, et al. Predictors of outcome in neck and shoulder symptoms: a cohort study in general practice. *Spine (Phila Pa 1976)*. 2005;30(16):E459-70. doi:00007632-200508150-00022 [pii].
10.   Cecchi F, Molino-Lova R, Paperini A, et al. Predictors of short- and long-term outcome in patients with chronic non-specific neck pain undergoing an exercise-based rehabilitation program: a prospective cohort study with 1-year follow-up. *Intern Emerg Med*. 2011;6(5):413-421. doi:10.1007/s11739-010-0499-x.
11.   Michaelson P, Sjolander P, Johansson H. Factors Predicting Pain Reduction in Chronic Back and Neck. *… Clin J pain*. 2004;20(6):447-454. http://journals.lww.com/clinicalpain/Abstract/2004/11000/Factors_Predicting_Pain_Reduction_in_Chronic_Back.10.aspx.
12.   De Pauw R, Kregel J, De Blaiser C, et al. Identifying prognostic factors predicting outcome in patients with chronic neck pain after multimodal treatment: A retrospective study. *Man Ther*. 2015;20(4):592-597. doi:10.1016/j.math.2015.02.001.
13.   Hanney WJ, Kolber MJ, George SZ, Young I, Patel CK, Cleland JA. Development of a preliminary clinical prediction rule to identify patients with neck pain that may benefit from a standardized program of stretching and muscle performance exercise: a prospective cohort study. *Int J Sports Phys Ther*. 2013;8(6):756-776. http://www.pubmedcentral.nih.gov/articlerender.fcgi?artid=3867069&tool=pmcentrez&rendertype=abstract. Accessed October 10, 2016.
14.   Walton DM, Macdermid JC, Giorgianni AA, Mascarenhas JC, West SC, Zammit CA. Risk factors for persistent problems following acute whiplash injury: update of a systematic review and meta-analysis. *J Orthop Sports Phys Ther*. 2013;43(2):31-43. doi:10.2519/jospt.2013.4507.
15.   Walton DM, Carroll LJ, Kasch H, et al. An Overview of Systematic Reviews on Prognostic Factors in Neck Pain: Results from the International Collaboration on Neck Pain (ICON) Project. *Open Orthop J*. 2013;7:494-505. doi:10.2174/1874325001307010494.
16.   Borghouts JA, Koes BW, Bouter LM. The clinical course and prognostic factors of non-

specific neck pain: a systematic review. *Pain*. 1998;77(1):1-13. http://www.ncbi.nlm.nih.gov/pubmed/9755013. Accessed October 10, 2016.

17. Atherton K, Wiles NJ, Lecky FE, et al. Predictors of persistent neck pain after whiplash injury. *Emerg Med J*. 2006;23(3):195-201. doi:10.1136/emj.2005.027102.

18. Croft PR, Lewis M, Papageorgiou AC, et al. Risk factors for neck pain: a longitudinal study in the general population. *Pain*. 2001;93(3):317-325. doi:S0304395901003347 [pii].

19. Saavedra-Hernández M, Castro-Sánchez AM, Cuesta-Vargas AI, Cleland JA, Fernández-de-las-Peñas C, Arroyo-Morales M. The contribution of previous episodes of pain, pain intensity, physical impairment, and pain-related fear to disability in patients with chronic mechanical neck pain. *Am J Phys Med Rehabil*. 2012;91(12):1070-1076. doi:10.1097/PHM.0b013e31827449a5.

20. Landers MR, Creger R V., Baker C V., Stutelberg KS. The use of fear-avoidance beliefs and nonorganic signs in predicting prolonged disability in patients with neck pain. *Man Ther*. 2008;13(3):239-248. doi:10.1016/j.math.2007.01.010.

21. MacDermid JC, Walton DM, Avery S, et al. Measurement properties of the neck disability index: a systematic review. *J Orthop Sports Phys Ther*. 2009;39(5):400-417. doi:10.2519/jospt.2009.2930.

22. Pietrobon R, Coeytaux RR, Carey TS, Richardson WJ, DeVellis RF. Standard scales for measurement of functional outcome for cervical pain or dysfunction: a systematic review. *Spine (Phila Pa 1976)*. 2002;27(5):515-522. doi:10.1097/00007632-200203010-00012.

23. Resnick DN. Subjective outcome assessments for cervical spine pathology: A narrative review.

24. Vernon H. The Neck Disability Index: State-of-the-Art, 1991-2008. *J Manipulative Physiol Ther*. 2008;31(7):491-502. doi:http://dx.doi.org/10.1016/j.jmpt.2008.08.006.

25. Cleland JA, Fritz JM, Whitman JM, Palmer JA. The Reliability and Construct Validity of the Neck Disability Index and Patient Specific Functional Scale in Patients With Cervical Radiculopathy. *Spine (Phila Pa 1976)*. 2006;31(5):598-602. doi:10.1097/01.brs.0000201241.90914.22.

26. Cleland JA, Childs JD, Whitman JM. Psychometric Properties of the Neck Disability Index and Numeric Pain Rating Scale in Patients With Mechanical Neck Pain. *Arch Phys Med Rehabil*. 2008;89(1):69-74. doi:http://dx.doi.org/10.1016/j.apmr.2007.08.126.

27. Vos C, Verhagen A, Koes B. Reliability and responsiveness of the Dutch version of the Neck Disability Index in patients with acute neck pain in general practice. *Eur Spine J*. 2006;15(11). doi:10.1007/s00586-006-0119-7.

28. Young IA, Cleland JA, Michener LA, Brown C. Reliability, Construct Validity, and Responsiveness of the Neck Disability Index, Patient-Specific Functional Scale, and Numeric Pain Rating Scale in Patients with Cervical Radiculopathy. *Am J Phys Med Rehabil*. 2010;89(10):831-839. doi:10.1097/PHM.0b013e3181ec98e6.

29. Young BA, Walker MJ, Strunce JB, Boyles RE, Whitman JM, Childs JD. Responsiveness of the Neck Disability Index in patients with mechanical neck disorders. *Spine J*. 2009;9(10):802-808. doi:http://dx.doi.org/10.1016/j.spinee.2009.06.002.

30. Jorritsma W, Dijkstra PU, de Vries GE, Geertzen JHB, Reneman MF. Detecting relevant changes and responsiveness of Neck Pain and Disability Scale and Neck Disability Index. *Eur Spine J*. 2012;21(12):2550-2557. doi:10.1007/s00586-012-2407-8.

31. Stratford P, Riddle D, Binkley J, Spadoni G, Westaway MD PB. Using the Neck Disability Index to make decisions concerning individual patients. *Physiother Canada*. 1999.

32. Cleland JA, Fritz JM, Whitman JM, Palmer JA. The reliability and construct validity of the Neck Disability Index and patient specific functional scale in patients with cervical radiculopathy. *Spine (Phila Pa 1976)*. 2006;31(5):598-602. doi:10.1097/01.brs.0000201241.90914.22.

33. Pool JJM, Ostelo RWJG, Hoving JL, Bouter LM, de Vet HCW. Minimal clinically important

change of the Neck Disability Index and the Numerical Rating Scale for patients with neck pain. *Spine (Phila Pa 1976)*. 2007;32(26):3047-3051. doi:10.1097/BRS.0b013e31815cf75b.

34. Domínguez-Almendros S, Benítez-Parejo N, Gonzalez-Ramirez AR. Efficacy of high-dose sublingual immunotherapy in children allergic to house dust mites in real-life clinical practice. *Allergol Immunopathol (Madr)*. 2011;39(5):1-6. doi:10.1016/j.aller.2011.05.002.

35. Katz MH. Multivariable Analysis: A Primer for Readers of Medical Research. *Ann Intern Med*. 2003;138(8):644-650. doi:10.7326/0003-4819-138-8-200304150-00012.

36. Beattie P, Nelson R. Clinical prediction rules: What are they and what do they tell us? *Aust J Physiother*. 2006;52:157-163. doi:10.1016/S0004-9514(06)70024-1.

37. Moons KGM, Royston P, Vergouwe Y, Grobbee DE, Altman DG. Prognosis and prognostic research: what, why, and how? *BMJ*. 2009;338:b375. http://www.ncbi.nlm.nih.gov/pubmed/19237405. Accessed March 8, 2017.

38. Mcginn TG, Guyatt GH, Wyer PC, Naylor CD, Stiell IG, Richardson WS. Users' Guides to the Medical Literature XXII: How to Use Articles About Clinical Decision Rules. *JAMA*. 2000;284284(11). doi:10.1001/jama.284.1.79.

39. Kelly J, Ritchie C, Sterling M. Clinical prediction rules for prognosis and treatment prescription in neck pain: A systematic review. 2016. doi:10.1016/j.math.2016.10.066.

40. Williamson E, Williams MA, Gates S, Lamb SE. Risk factors for chronic disability in a cohort of patients with acute whiplash associated disorders seeking physiotherapy treatment for persisting symptoms. *Physiotherapy*. 2015;101(1):34-43. doi:10.1016/j.physio.2014.04.004.

41. Nederhand MJ, Ijzerman MJ, Hermens HJ, Turk DC, Zilvold G. Predictive Value of Fear Avoidance in Developing Chronic Neck Pain Disability: Consequences for Clinical Decision Making. doi:10.1016/j.apmr.2003.06.019.

42. Ritchie C, Hendrikz J, Kenardy J, Sterling M. Derivation of a clinical prediction rule to identify both chronic moderate/ severe disability and full recovery following whiplash injury. *Pain*. 2013;154:2198-2206. doi:10.1016/j.pain.2013.07.001.

43. Ritchie C, Hendrikz J, Jull G, Elliott J, Sterling M. External Validation of a Clinical Prediction Rule to Predict Full Recovery and Ongoing Moderate/Severe Disability Following Acute Whiplash Injury. *J Orthop Sport Phys Ther*. 2015;45(4):242-250. doi:10.2519/jospt.2015.5642.

44. Dagfinrud H, Storheim K, Magnussen LH, et al. The predictive validity of the Örebro Musculoskeletal Pain Questionnaire and the clinicians' prognostic assessment following manual therapy treatment of patients with LBP and neck pain. *Man Ther*. 2013;18:124-129. doi:10.1016/j.math.2012.08.002.

45. Kasch H, Qerama E, Kongsted A, Bendix T, Jensen TS, Bach FW. Clinical assessment of prognostic factors for long-term pain and handicap after whiplash injury : a 1-year prospective study. 2008:1222-1230. doi:10.1111/j.1468-1331.2008.02301.x.

46. Schellingerhout JM, Heymans MW, Verhagen AP, Lewis M, de Vet HCW, Koes BW. Prognosis of patients with nonspecific neck pain: development and external validation of a prediction rule for persistence of complaints. *Spine (Phila Pa 1976)*. 2010;35(17):E827-35. doi:10.1097/BRS.0b013e3181d85ad5.

47. Radanov BP, Sturzenegger M. Predicting Recovery from Common Whiplash. *Eur Neurol*. 2008;36(1):48-51. doi:10.1159/000117200.

48. Kasch H, Qerama E, Kongsted A, Bach FW, Bendix T, Jensen TS. The Risk Assessment Score in Acute Whiplash Injury Predicts Outcome and Reflects Biopsychosocial Factors. *Spine (Phila Pa 1976)*. 2011;36(25 Suppl):S263-S267. doi:10.1097/BRS.0b013e31823881d6.

49. Kasch H, Kongsted A, Qerama E, Bach FW, Bendix T, Staehelin Jensen T. A new stratified risk assessment tool for whiplash injuries developed from a prospective

observational study. doi:10.1136/.

50. Carroll LJ, Cassidy JD, Cô Té P. The role of pain coping strategies in prognosis after whiplash injury: Passive coping predicts slowed recovery. doi:10.1016/j.pain.2006.03.012.

51. Cleland, Joshua a, Childs, Fritz, Whitman E. Development of a clinical prediction rule for guiding treatment of a subgroup of patients with neck pain: Use of thoracic spine manipulation, excercise and patient education. 2007. doi:10.2522/ptj.20060155.

52. Gabel CP, Burkett B, Neller A, Yelland M. Can long-term impairment in general practitioner whiplash patients be predicted using screening and patient-reported outcomes? *Int J Rehabil Res*. 2008;31(1):79-80. doi:10.1097/MRR.0b013e3282f44e10.

53. Grotten WJA, Mulder M, Josephson M, Alfredsson L, Wiktorin C. The influence of work-related exposures on the prognosis of neck/shoulder pain. doi:10.1007/s00586-007-0481-0.

54. Hartling L, Pickett W, Brison RJ. Derivation of a clinical decision rule for whiplash associated disorders among individuals involved in rear-end collisions. *Accid Anal Prev*. 2002;34:531-539. www.elsevier.com/locate/aap. Accessed March 8, 2017.

55. Kasch H, FW B, TS J. Handicap after acute whiplash injury: A 1-year prospective study of risk factors. *Neurology*. 2001;56(12):1637-1643.

56. Landers MR, Creger R V., Baker C V., Stutelberg KS. The use of fear-avoidance beliefs and nonorganic signs in predicting prolonged disability in patients with neck pain. *Man Ther*. 2008;13(3):239-248. doi:10.1016/j.math.2007.01.010.

57. Vos CJ, Verhagen AP, Koes BW. THE ABILITY OF THE ACUTE LOW BACK PAIN SCREENING QUESTIONNAIRE TO PREDICT SICK LEAVE IN PATIENTS WITH ACUTE NECK PAIN. *J Manipulative Physiol Ther*. 32:178-183. doi:10.1016/j.jmpt.2009.02.004.