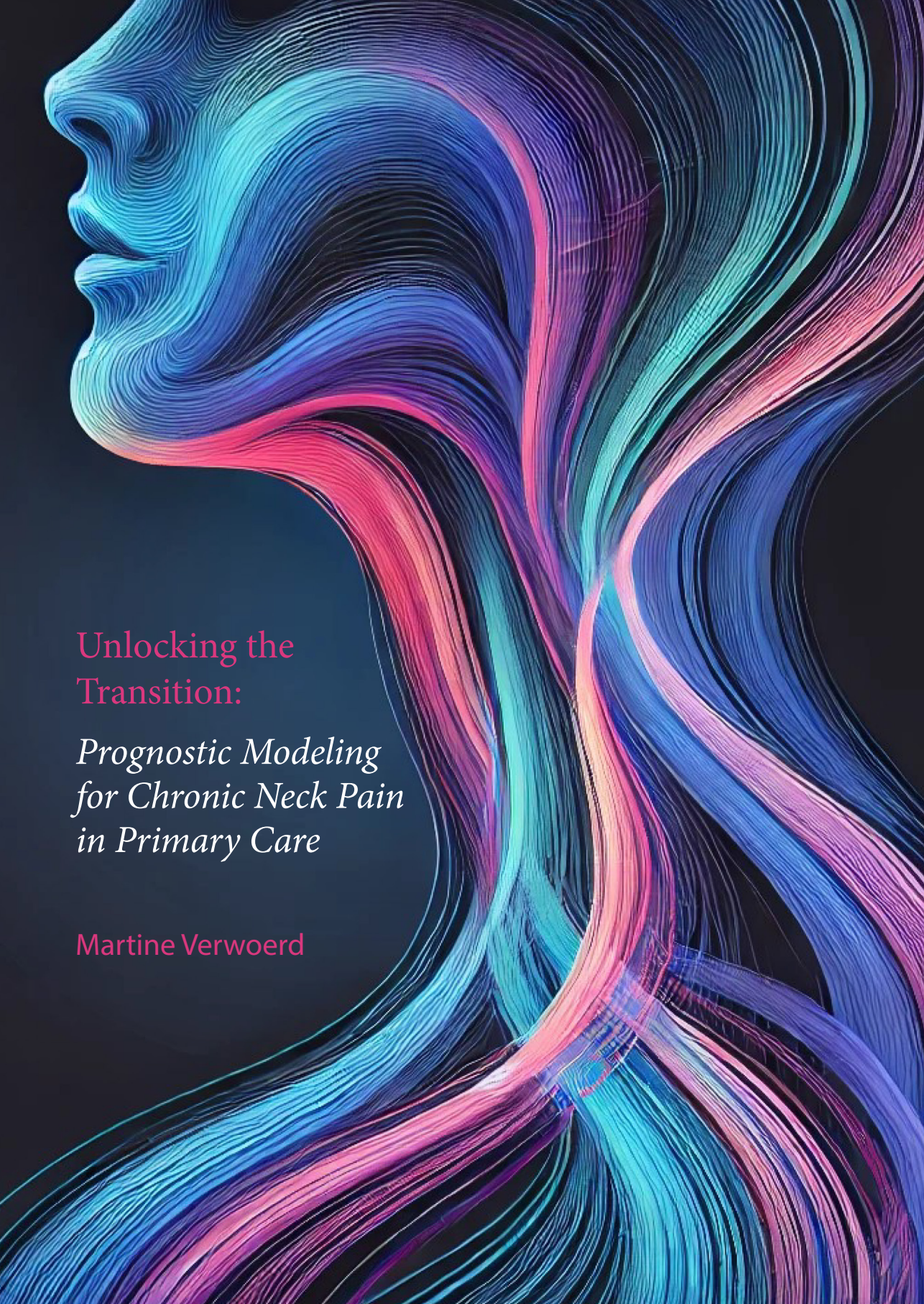




Unlocking the
Transition:

*Prognostic Modeling
for Chronic Neck Pain
in Primary Care*

Martine Verwoerd

Unlocking the Transition:

Prognostic Modeling for Chronic Neck Pain in Primary Care

Martine Verwoerd

Cover	Martine Verwoerd and ChatGPT
Layout	Renate Siebes Proefschrift.nu
Printed by	Proefschriftmaken.nl www.proefschriftmaken.nl
ISBN	978-94-6510-332-7

© **Copyright Martine Verwoerd, 2024, the Netherlands.**

All rights reserved. No part of this doctoral dissertation may be duplicated, stored in a retrieval system, or transmitted in any form or by any means, without the prior written permission from the author or the copyright-owning journal.

Unlocking the Transition:

Prognostic Modeling for Chronic Neck Pain in Primary Care

DISSERTATION

to obtain the degree of Doctor at Maastricht University,
on the authority of the Rector Magnificus, Prof. Dr. Pamela Habibović
in accordance with the decision of the Board of Deans,
to be defended in public on
Wednesday 18 December 2024, at 10.00 hours

by

Martine Janine Verwoerd

Supervisor:

Prof. Dr. Rob J.E.M. Smeets, Maastricht University

Co-supervisor:

Dr. Harriët Wittink, University of Applied Sciences Utrecht

Assessment Committee:

Prof. Dr. Paul C. Willems (chair), Maastricht University

Dr. Brona Fullen, University College, Dublin, Ireland

Prof. Dr. Madelon L. Peters, Maastricht University

Prof. Dr. Cindy Veenhof, UMC Utrecht

Prof. Dr. Jan H.M. van Zundert, Maastricht University

This doctoral thesis was a collaboration between the Lifestyle & Health research group (Department for Healthy and Sustainable Living) at the University of Applied Sciences Utrecht and the department of Rehabilitation Medicine (Care and Public Health Research Institute CAPHRI) at Maastricht University.

Contents

Chapter 1	General introduction	7
<i>Part 1</i>		
Chapter 2	Prognostic factors for persistent pain after a first episode of nonspecific idiopathic, non-traumatic neck pain: A systematic review	23
Chapter 3	Consensus of potential modifiable prognostic factors for persistent pain after a first episode of nonspecific idiopathic, non-traumatic neck pain: results of nominal group and Delphi technique approach	77
<i>Part 2</i>		
Chapter 4	A study protocol for the validation of a prognostic model with an emphasis on modifiable factors to predict chronic pain after a new episode of acute- or subacute nonspecific idiopathic, non-traumatic neck pain presenting in primary care	127
Chapter 5	Development and internal validation of a multivariable prognostic model to predict chronic pain after a new episode of non-specific idiopathic, non-traumatic neck pain in physiotherapy primary care practice	153
Chapter 6	Evaluating clinical characteristics and the impact of pain severity on functionality and psychological well-being in non-specific neck pain: A study in primary physiotherapy care	189
<i>Part 3</i>		
Chapter 7	Physiotherapists' knowledge, attitude and practice behavior to prevent chronification in patients with non-specific, non-traumatic, acute- and subacute neck pain: A qualitative study	227
Chapter 8	General discussion	257
	Summary	279
	Nederlandse samenvatting (Summary in Dutch)	287
	Author affiliations	295
	Dankwoord (Acknowledgements)	299
	About the author	309
	Curriculum vitae	311
	Publications	312





Chapter 1

General introduction

General introduction

As a physiotherapist within primary care practice, I consistently encountered two critical sources of inquiry that drove my research ambitions. Firstly, patients enduring acute and subacute episodes of neck pain frequently presented with a pressing question: ‘How long will it take for me to recover?’. This query reflects the concerns and urgency of those suffering from neck pain and underscores the necessity for a profound understanding of recovery trajectories within this field. Secondly, there was an intuitive layer to my patient evaluations beyond the empirical knowledge of expected recovery timelines. Often, I believed in anticipations about certain patients’ recovery prospects—foreseeing, in some instances, that a patient might not fully recover, potentially developing chronic pain, or expecting significantly less benefit from my interventions. This duality of precise knowledge and intuitive speculation prompted a critical self-inquiry: on what basis were these intuitions founded? Were there detectable patterns or identifiable indicators that could systematically support or refute my intuitive judgements?

These dual motivations—stemming from direct patient queries and my introspective reflection on the accuracy of my clinical intuitions—have driven me towards prognostic research. This thesis embarks on this exploration, aiming to unravel the complexities surrounding the prognosis of (sub) acute neck pain.

Neck pain

Neck pain is a prevalent and debilitating health condition that substantially impacts public health and economic consequences.^{1,2} Acknowledged as the third leading cause of ‘years lived with disability’ among non-fatal diseases in Europe, neck pain afflicts an estimated 15 to 18% of the general population each year.^{3–5} Worldwide, the prevalence of neck pain varies, ranging from 16% to 75%.⁶ Neck pain is a multifaceted biopsychosocial disorder that significantly affects individuals’ quality of life, work productivity, daily activities, and social and psychological well-being.^{7,8} Given the high prevalence of neck pain, it is likely that most adults will experience neck pain at some point in their lives. In the Netherlands, neck pain is one of the most common musculoskeletal disorders encountered in primary physiotherapy practices.

Non-specific neck pain

Non-specific neck pain is characterized by pain or discomfort in and around the neck and shoulder girdle, typically perceived in the posterior region of the cervical spine, extending from the superior nuchal line to the first thoracic spinous process.⁹ It may radiate to the head, trunk and upper limbs and can occur with or without a concurrent loss of movement of the cervical spine.¹⁰ This condition is distinguished by the absence of an identifiable specific cause or pathoanatomical aberrations, such as nerve root compression, trauma, fracture, malignancy, infection, inflammatory arthritis), or neurological diseases.¹¹ To aid in assessing and managing non-specific neck pain, the Bone and Joint Decade 2000–2010 Task Force on Neck Pain and its Associated Disorders (Scientific Secretariat and Advisory Committee) recommends a four-grade classification system for neck pain severity.¹⁰ No indications of significant pathology and minimal disruption of daily activities characterize grade 1 neck pain. In contrast, grade 2 neck pain, while also indicating an absence of major pathology, is characterized by a more significant interference with daily activities. This dissertation concentrates on grades 1 and 2 of this classification system, as grade 3 and 4 neck pain no longer fall under the category of non-specific neck pain. Grade 3 neck pain, though showing no signs of significant pathology, is accompanied by neurological symptoms suggestive of nerve compression, such as reduced deep tendon reflexes, muscle weakness, or sensory deficits. Signs of substantial structural pathology mark grade 4 neck pain, necessitating immediate investigation and treatment. Although the precise aetiology of non-specific neck pain remains unknown, it is broadly considered multifactorial.¹⁰ Contemporary clinical guidelines advocate for a multimodal assessment and management approach in addressing non-specific neck pain in physiotherapy.¹²

Transition from acute to chronic pain

Pain

The International Association for the Study of Pain (IASP) defines pain as “an unpleasant sensory and emotional experience associated with, or resembling that associated with, actual or potential tissue damage”.¹³ Keynotes underlying the current definition of pain are: (1) pain is always a personal experience that is influenced to varying degrees by biological, psychological, and social factors; (2) pain and nociception are different phenomena – pain cannot be inferred solely

from activity in sensory neurons, (3) although pain usually serves an adaptive role, it may have adverse effects on function and social and psychological well-being.¹³

Acute pain

Acute pain is characterized as a sudden onset of sharp or intense pain as a warning sign of disease or bodily threat. Typical causes of acute pain include injuries, illness, trauma, or painful medical interventions such as surgery. Acute pain generally disappears once the underlying cause is treated or the induced injury has healed.¹⁴ Although acute trauma is often linked to pain, musculoskeletal neck pain usually occurs from everyday activities; this includes sustained static positions, cumulative small amplitude forces occurring with overexertion, repetitive activities, and forceful actions.¹⁵

Chronic pain

As defined by Treede et al. (2015), chronic musculoskeletal pain is the perception of pain in musculoskeletal tissues persisting or recurring for more than three months.¹⁶ This duration typically exceeds the average tissue healing time and is characterized by significant functional disability and emotional distress.¹⁶ Chronic pain is categorized into two types: primary chronic pain, which cannot be directly attributed to a known disease or damage process, and secondary chronic pain, resulting from a disease or process that directly affects the bones, joints, muscles, and related soft tissues.¹⁷

The focus of this dissertation is on the development of primary chronic pain. The common thread of chronic pain is its pervasive impact on daily life, manifesting as activity limitation and emotional distress. Chronic musculoskeletal pain, in particular, has a substantial social and emotional effect, which may encompass decreased socialization, inability to work, loss of independence, and the development of psychological conditions such as anxiety and depression, alongside concerns about the future.^{18,19}

Pathophysiology of the transition of acute to chronic pain

The precise pathophysiology mechanisms underlying musculoskeletal pain remain not fully understood.²⁰ However, factors such as inflammation, fibrosis, tissue degradation, and neurosensory changes are recognized as contributors.²¹ Tissue injuries increase pro-inflammatory cytokines and mediators within the affected

tissues, potentially leading to the sensitization of peripheral nociceptors.²² Inflammation may prompt fibrotic scarring, impeding the smooth gliding of tissues during movement and increasing tissue strain due to adhesion with adjacent structures, consequently exacerbating pain.²³ The increase of inflammatory mediators also promotes the production of matrix metalloproteinases, which reduces the tolerance of tissues to load, potentially causing further damage and amplified pain.²⁴ Additionally, the levels of neurotransmitters, such as substance P and calcitonin-related peptide, tend to increase in the impacted tissues, dorsal root ganglia, and dorsal horns of the spinal cord, contributing to either the sensitization of peripheral nociceptors or a central amplification of pain.^{20,25}

The activation of nociceptors initiates a complex engagement of extensive neural networks within the brain, transforming sensory input into the subjective experience of pain.^{20,25} This process involves complex interactions among higher brain regions, likely revealing insights into the mechanisms of chronification of musculoskeletal pain. Central to this is descending inhibition, which is fundamental in determining the transition from acute to chronic pain. A robust descending inhibitory system acts protectively against the development of chronic pain.^{20,25} Key brain areas in this modulatory system include higher cortical and subcortical centers, such as the prefrontal cortex and the limbic system.²⁵ These centers are responsible for encoding a range of processes. Their function extends to cognition, emotion, motivation, and sensation, and they are functionally connected to the descending pain modulatory circuits.²⁵ The dynamic interplay between these brain regions and the descending pain modulatory pathways facilitates how emotional and motivational factors can significantly alter pain perception and experience.²⁵ The apparent loss of descending inhibition promotes chronic pain, while the engagement of inhibition protects against it. An imbalance between the inhibitory and facilitatory components of the descending pain modulatory systems may underlie the chronification of musculoskeletal pain.

Biopsychosocial factors in the experience of pain

The perception of pain inherently requires our focus on the noxious stimulus. Pain naturally commands our attention, serving a beneficial purpose by initiating responses to potential threats.²⁶ Attention and pain are closely intertwined with emotional and cognitive processes.²⁷ Upon detecting a noxious stimulus, our cognitive abilities are used to understand what the stimuli mean. This interpreta-

tion is directly linked with emotional responses and influences our subsequent behavior.²⁷ Beliefs play an essential role in making sense of a stimulus; they act as cognitive shortcuts, enabling the brain to process vast amounts of information efficiently.^{28,29} These beliefs and attitudes are further shaped by our social environment, indicating that perceptions about the causes of our pain and its appropriate treatment are influenced by the society in which we live.²⁸ Certain beliefs, particularly those that lead to activity limitation, are associated with the development of chronic pain and disability.²⁷

Understanding pain involves not only fundamental cognitive and emotional elements but also necessitates a biopsychosocial approach when considering prognostic factors for the chronification of pain.³⁰ This comprehensive perspective underscores the importance of recognizing how a constellation of interrelated biopsychosocial factors contributes to the development of chronic pain, thereby inherently leading to an exhaustive assessment of all aspects of the biopsychosocial model.³¹

Biological, often called physical factors, encompass various elements, from genetics and neurobiology to lifestyle influences. These can include the magnitude of nociception, tissue injury, physical health issues, immune function, neurochemical changes, effects of medications, and differences in sex and nervous system characteristics such as pain threshold and tolerance.³² Additionally, factors like hormones, lifestyle choices (e.g., sleep, weight, food, physical activity, alcohol, smoking or substance abuse), and endogenous pain modulation systems play a role.³² Biomechanics and physical fitness are critical components, including endurance, strength, and flexibility.³²

Psychological factors delve into the field of cognition and emotions. These include mood, depression, anxiety, distress, anger, perceived injustice, and coping styles like avoidance or endurance.^{32,33} Fear, self-efficacy, catastrophizing, personality traits, beliefs about the causes and consequences of pain, resilience, attitudes, acceptance, and expectancies about recovery are all integral to how pain is experienced and managed by the individual.^{32,33}

Lastly, social or sociocultural factors encompass various elements that influence pain experience. These include social expectations, support systems (financial, instrumental, and emotional support), educational status, living conditions, work-related issues, economic circumstances, and broader societal issues such as social deprivation, poverty, social disadvantage, exclusion, and past pain experiences.³²

Additional considerations include health insurance, disability compensation, language and cultural barriers, stigma, discrimination, and overall cultural factors.³²

Together, these biopsychosocial factors provide a comprehensive framework for understanding the complex nature of pain experience. As many authors have debated, it is not solely the nervous system that endures chronic pain but rather the individual interacting with their social context.^{34,35} Hence, the transition from acute to chronic pain must be considered from psychological and social perspectives, in addition to the biological perspective.

Health care providers

Patients experiencing pain frequently interact with a variety of healthcare providers. This often involves a physiotherapist in cases of (sub)acute neck pain. These providers, particularly physiotherapists, are essential in managing neck pain patients. Consequently, they may be influential external factors in transitioning from acute to chronic neck pain. As previously discussed, incorporating biological, psychological, and social factors in assessing and treating patients with neck pain is essential. Physiotherapy has undergone a paradigm shift over time, transitioning from a predominantly biological focus to a biopsychosocial approach.³⁶ However, the integration of psychological knowledge into the clinical practice of physiotherapy remains a substantial challenge.³⁷ Therefore, alongside investigating prognostic factors within a biopsychosocial framework, it is crucial to examine primary care physiotherapists' current knowledge, attitudes, and clinical behaviors when assessing and treating patients with (sub)acute neck pain.

Prognostic research in the context of chronification of neck pain

Prognostic research fundamentally concerns the study of future health outcomes in individuals with specific diseases or health conditions, notably neck pain.³⁸ This field of inquiry delves into predicting these outcomes on a given baseline individual health status.³⁹ Prognostic research spans from overarching prognoses, such as the chronification of neck pain in the population, to prognostic factor analyses, which involve research on the factors associated with changes in prognosis and what is meaningful for an individual.⁴⁰ It further extends to prognostic modelling, integrating multiple factors to predict the risk of future clinical outcomes in individual patients.⁴¹ A useful prognostic model provides accurate predictions that inform

patients and their caregivers, guide treatment decisions, allow for more informed shared decision-making, and support clinical research (e.g. trial randomization).⁴¹

Aims and outline of this thesis

This dissertation aims to enhance our understanding of the prognosis of non-specific, non-traumatic neck pain while also examining primary care physiotherapists' perceptions and approaches to managing this condition. The central question of this dissertation is: Can we predict which patients will develop chronic neck pain? To address this question comprehensively, the dissertation is organized into three parts, each corresponding to a specific sub-question:

Part 1 addresses the sub-question: What factors should be measured to predict the chronicity of neck pain? This part begins with an in-depth analysis of existing knowledge and scholarly consensus on prognostic factors that influence the chronification of non-specific neck pain.

Part 2 explores the sub-question: Which factors are prognostic for the chronification of neck pain? It features a detailed longitudinal prognostic study, evaluating the prognostic value of various factors associated with acute and subacute non-specific neck pain.

Part 3 examines the sub-question: What are physiotherapists' perspectives on these prognostic factors and their impact on clinical practices? This part transitions into physiotherapy practice, studying physiotherapists' knowledge, attitudes, and clinical behaviors concerning non-specific neck pain, and how these professionals integrate prognostic factors into their patient management strategies.

This thesis aims to bridge gaps in current research and provides a detailed framework for future studies and clinical practices in physiotherapy.

Detailed chapter descriptions

Chapter 2: Systematic review of prognostic factors for chronification of neck pain

This chapter details the outcomes of a systematic review analyzing the current state of literature, focusing on identifying and synthesizing modifiable and non-modifiable prognostic factors relevant to the chronification of neck pain.

Chapter 3: Consensus on modifiable prognostic factors for chronification of neck pain

This chapter presents a consensus on potential modifiable prognostic factors for developing chronic neck pain, utilizing a modified Nominal Group Technique and a Delphi survey to lay the groundwork for a comprehensive longitudinal cohort study.

Chapter 4: Development of a prognostic model for neck pain chronification

This chapter describes a research protocol for developing and internally validating a prognostic model for the chronification of neck pain. It focuses on the methodological approach and foundational elements of model development.

Chapter 5: Longitudinal cohort study and prognostic model validation

This chapter presents the results of the longitudinal cohort study, specifically focusing on an internally validated prognostic model.

Chapter 6: Evaluating the clinical characteristics and the impact of pain severity on functionality and psychological well-being

This chapter evaluates the clinical characteristics of patients experiencing their first episode of NSNP and patients with a new episode of NSNP in a recurrent pattern, as well as the impact of neck pain severity on functionality and emotional well-being.

Chapter 7: Physiotherapist knowledge, attitude and behavior regarding neck pain

This chapter investigates physiotherapists' knowledge, attitudes, and practice behavior in assessing and managing patients with acute and subacute non-traumatic neck pain, highlighting the significance of a holistic approach in patient care.

Chapter 8: General discussion, considerations, and recommendations

This final chapter synthesizes the thesis's main findings and offers considerations and recommendations for clinical practice and future research directions.

References

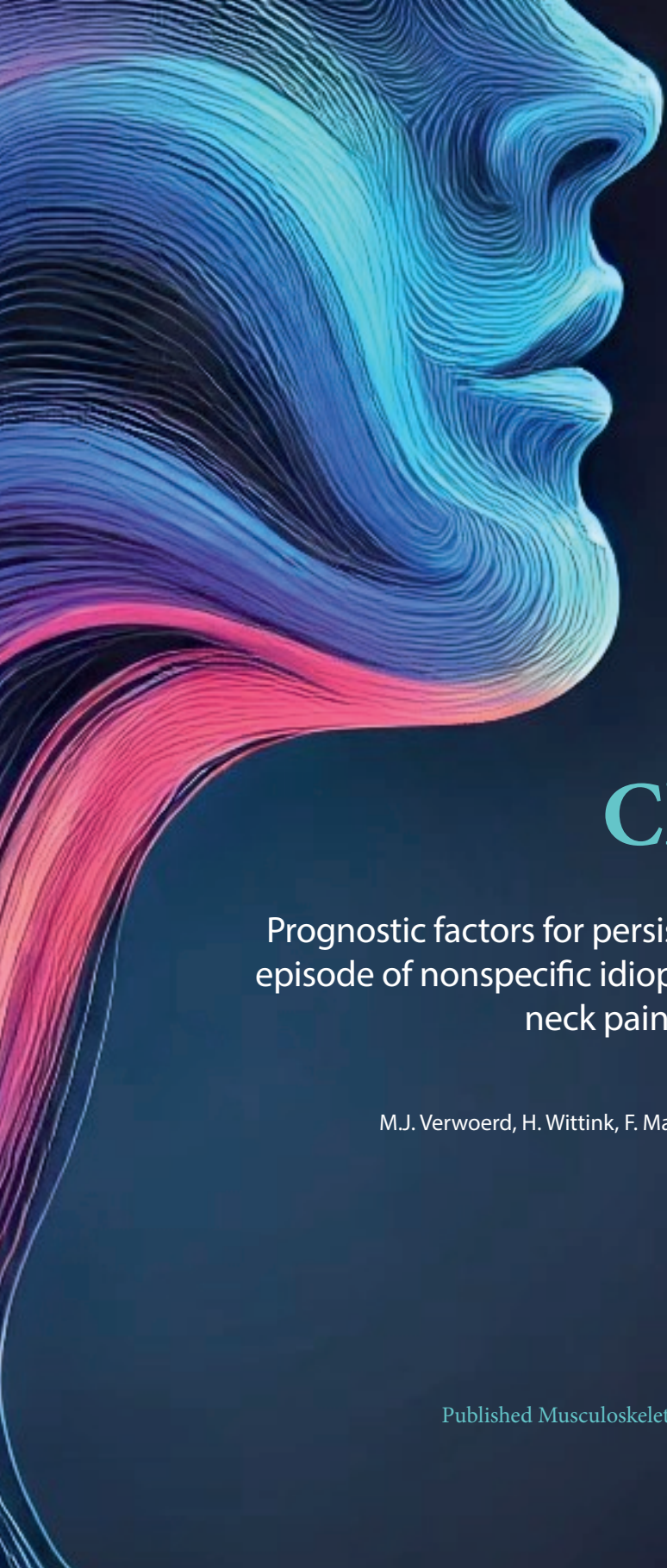
1. Carroll LJ, Hogg-Johnson S, van der Velde G, et al. Course and Prognostic Factors for Neck Pain in the General Population. *European Spine Journal*. 2008;17:75–82. doi: 10.1007/s00586-008-0627-8
2. Lee H, Hübscher M, Moseley GL, et al. How does pain lead to disability? A systematic review and meta-analysis of mediation studies in people with back and neck pain. *Pain*. 2015;156:988–97. doi: 10.1097/j.pain.0000000000000146
3. GBD 2015 Disease and Injury Incidence and Prevalence Collaborators G 2015 D and II and P. Global, regional, and national incidence, prevalence, and years lived with disability for 310 diseases and injuries, 1990–2015: a systematic analysis for the Global Burden of Disease Study 2015. *Lancet*. 2016;388:1545–602. doi: 10.1016/S0140-6736(16)31678-6
4. Côté P, Cassidy DJ, Carroll LJ, et al. The annual incidence and course of neck pain in the general population: a population-based cohort study. *Pain*. 2004;112:267–73. doi: 10.1016/j.pain.2004.09.004
5. Croft PR, Lewis M, Papageorgiou AC, et al. Risk factors for neck pain: a longitudinal study in the general population. *Pain*. 2001;93:317–25. doi: 10.1016/S0304-3959(01)00334-7
6. Fejer R, Kyvik KO, Hartvigsen J. The prevalence of neck pain in the world population: a systematic critical review of the literature. *European Spine Journal*. 2006;15:834–48. doi: 10.1007/s00586-004-0864-4
7. Côté P, Wong JJ, Sutton D, et al. Management of neck pain and associated disorders: A clinical practice guideline from the Ontario Protocol for Traffic Injury Management (OPTiMa) Collaboration. *European Spine Journal*. 2016;25:2000–22. doi: 10.1007/s00586-016-4467-7
8. Genebra CVDS, Maciel NM, Bento TPE, et al. Prevalence and factors associated with neck pain: a population-based study. *Braz J Phys Ther*. 2017;21:274–80. doi: 10.1016/j.bjpt.2017.05.005
9. Misailidou V, Malliou P, Beneka A, et al. Assessment of patients with neck pain: a review of definitions, selection criteria, and measurement tools. *J Chiropr Med*. 2010;9:49–59. doi: 10.1016/j.jcm.2010.03.002
10. Guzman J, Hurwitz EL, Carroll LJ, et al. A New Conceptual Model of Neck Pain. *J Manipulative Physiol Ther*. 2009;32:S17–28. doi: 10.1016/j.jmpt.2008.11.007
11. Domingues L, Cruz EB, Pimentel-Santos FM, et al. Prognostic factors for recovery and non-recovery in patients with non-specific neck pain: a protocol for a systematic literature review. *BMJ Open*. 2018;8:e023356. doi: 10.1136/bmjopen-2018-023356
12. Kjaer P, Kongsted A, Hartvigsen J, et al. National clinical guidelines for non-surgical treatment of patients with recent onset neck pain or cervical radiculopathy. *European Spine Journal*. 2017;26:2242–57. doi: 10.1007/s00586-017-5121-8
13. Raja SN, Carr DB, Cohen M, et al. The revised International Association for the Study of Pain definition of pain: concepts, challenges, and compromises. *Pain*. 2020;161:1976–82. doi: 10.1097/j.pain.0000000000001939
14. <https://www.iasp-pain.org/resources/topics/acute-pain/>.
15. Puntillo F, Giglio M, Paladini A, et al. Pathophysiology of musculoskeletal pain: a narrative review. *Ther Adv Musculoskelet Dis*. 2021;13:1759720X2199506. doi: 10.1177/1759720X21995067

- 16 Treede R-D, Rief W, Barke A, et al. A classification of chronic pain for ICD-11. *Pain*. 2015;156:1003–7. doi: 10.1097/j.pain.0000000000000160
- 17 Perrot S, Cohen M, Barke A, et al. The IASP classification of chronic pain for ICD-11: chronic secondary musculoskeletal pain. *Pain*. 2019;160:77–82. doi: 10.1097/j.pain.0000000000001389
- 18 Duenas M, Ojeda B, Salazar A, et al. A review of chronic pain impact on patients, their social environment and the health care system. *J Pain Res*. 2016;9:457–67. doi: 10.2147/JPR.S105892
- 19 Garnæs KK, Mørkved S, Tønne T, et al. Mental health among patients with chronic musculoskeletal pain and its relation to number of pain sites and pain intensity, a cross-sectional study among primary health care patients. *BMC Musculoskelet Disord*. 2022;23:1115. doi: 10.1186/s12891-022-06051-9
- 20 Ossipov MH, Morimura K, Porreca F. Descending pain modulation and chronification of pain. *Curr Opin Support Palliat Care*. 2014;8:143–51. doi: 10.1097/SPC.0000000000000055
- 21 Barr AE, Barbe MF. Inflammation reduces physiological tissue tolerance in the development of work-related musculoskeletal disorders. *Journal of Electromyography and Kinesiology*. 2004;14:77–85. doi: 10.1016/j.jelekin.2003.09.008
- 22 Lutke Schipholt IJ, Coppieters MW, Diepens M, et al. Systemic Inflammation, Sleep, and Psychological Factors Determine Recovery Trajectories for People With Neck Pain: An Exploratory Study. *J Pain*. 2024;25:104496. doi: 10.1016/j.jpain.2024.02.010
- 23 Driscoll M, Blyum L. The presence of physiological stress shielding in the degenerative cycle of musculoskeletal disorders. *J Bodyw Mov Ther*. 2011;15:335–42. doi: 10.1016/j.jbmt.2010.05.002
- 24 Barbe MF, Gallagher S, Massicotte VS, et al. The interaction of force and repetition on musculoskeletal and neural tissue responses and sensorimotor behavior in a rat model of work-related musculoskeletal disorders. *BMC Musculoskelet Disord*. 2013;14:303. doi: 10.1186/1471-2474-14-303
- 25 Tracey I, Mantyh PW. The Cerebral Signature for Pain Perception and Its Modulation. *Neuron*. 2007;55:377–91. doi: 10.1016/j.neuron.2007.07.012
- 26 Linton SJ, Shaw WS. Impact of Psychological Factors in the Experience of Pain. *Phys Ther*. 2011;91:700–11. doi: 10.2522/ptj.20100330
- 27 Nicholas MK, Linton SJ, Watson PJ, et al. Early Identification and Management of Psychological Risk Factors (“Yellow Flags”) in Patients With Low Back Pain: A Reappraisal. *Phys Ther*. 2011;91:737–53. doi: 10.2522/ptj.20100224
- 28 Caneiro JP, Bunzli S, O’Sullivan P. Beliefs about the body and pain: the critical role in musculoskeletal pain management. *Braz J Phys Ther*. 2021;25:17–29. doi: 10.1016/j.bjpt.2020.06.003
- 29 Leventhal H, Phillips LA, Burns E. The Common-Sense Model of Self-Regulation (CSM): a dynamic framework for understanding illness self-management. *J Behav Med*. 2016;39:935–46. doi: 10.1007/s10865-016-9782-2
- 30 Treede R-D, Rief W, Barke A, et al. Chronic pain as a symptom or a disease: the IASP Classification of Chronic Pain for the International Classification of Diseases (ICD-11). *Pain*. 2019;160:19–27. doi: 10.1097/j.pain.0000000000001384
- 31 Fillingim RB. Individual differences in pain: understanding the mosaic that makes pain personal. *Pain*. 2017;158:S11–8. doi: 10.1097/j.pain.0000000000000775

- 32 European Pain Federation EFIC. <https://europeanpainfederation.eu/what-is-the-bio-psycho-social-model-of-pain/>.
- 33 Nicholas MK. The biopsychosocial model of pain 40 years on: time for a reappraisal? *Pain*. 2022;163:S3–14. doi: 10.1097/j.pain.0000000000002654
- 34 Eccleston C. Chronic pain as embodied defence: implications for current and future psychological treatments. *Pain*. 2018;159:S17–23. doi: 10.1097/j.pain.0000000000001286
- 35 Thacker MA, Moseley GL. First-person neuroscience and the understanding of pain. *Medical Journal of Australia*. 2012;196:410–1. doi: 10.5694/mja12.10468
- 36 Daluiso-King G, Hebron C. Is the biopsychosocial model in musculoskeletal physiotherapy adequate? An evolutionary concept analysis. *Physiother Theory Pract*. 2022;38:373–89. doi: 10.1080/09593985.2020.1765440
- 37 van Dijk H, Köke AJA, Elbers S, et al. Physiotherapists Using the Biopsychosocial Model for Chronic Pain: Barriers and Facilitators—A Scoping Review. *Int J Environ Res Public Health*. 2023;20:1634. doi: 10.3390/ijerph20021634
- 38 Riley RD, van der Windt DA, Croft P, Moons KGM. *Prognosis research in healthcare Concepts, Methods, and Impact*. 1st ed. Oxford: Oxford University Press 2019.
- 39 Hemingway H, Croft P, Perel P, et al. Prognosis research strategy (PROGRESS) 1: A framework for researching clinical outcomes. *BMJ (Online)*. 2013;346:1–11. doi: 10.1136/bmj.e5595
- 40 Riley RD, Hayden JA, Steyerberg EW, et al. Guidelines and Guidance Prognosis Research Strategy (PROGRESS) 2: Prognostic Factor Research. *PLoS Med*. 2013;10:e1001380. doi: 10.1371/journal.pmed.1001380
- 41 Steyerberg EW, Moons KGM, van der Windt DA, Hayden JA, Perel P, et al. Prognosis Research Strategy (PROGRESS) 3: Prognostic Model Research. *PLoS Med*. 2013;10:e1001381. doi: <https://doi.org/10.1371/journal.pmed.1001381>

Part 1





Chapter 2

Prognostic factors for persistent pain after a first episode of nonspecific idiopathic, non-traumatic neck pain: A systematic review

M.J. Verwoerd, H. Wittink, F. Maissan, E. de Raaij, R.J.E.M. Smeets

Published Musculoskeletal Science and Practice, 2019, July

Background: Prognosis of acute idiopathic neck pain is poor. An overview of modifiable and non-modifiable prognostic factors for the development of chronic musculoskeletal neck pain after an episode of idiopathic, non-traumatic neck pain is needed.

Objective: Identify prognostic factors for pain intensity and perceived non-recovery at three, six and 12 months after a first episode of idiopathic, non-traumatic neck pain.

Study design: Systematic review

Methods: Systematic literature search up to October 21, 2017 for prospective prognostic studies with main outcomes perceived non-recovery and pain intensity. The QUIPS was used for quality assessment.

Results: Out of 2,737 screened articles six prospective studies with high-risk-of-bias were identified, analyzing 47 and 43 factors for the outcome variables 'pain intensity' and 'perceived non-recovery', respectively. Based on univariate and multivariate analyses we found moderate evidence for 'age > 40 years' and 'concomitant back pain' to be prognostic for 'pain intensity'. For the outcome 'perceived non-recovery' at 12 months, we found moderate evidence for both 'a previous period of neck pain' and 'accompanying headache' as prognostic variables for persistent pain, based on univariate analysis. No prognostic factor was found which was retained in more than one multivariate analysis for the outcome variable 'perceived non-recovery'. However, the quality of the evidence for these prognostic factors was low to very low.

Conclusion: This review identifies prognostic factors for neck pain, of which only a few are modifiable. Further research is needed before drawing definite conclusions about the prognostic value of these factors.

Key words: Chronic neck pain, idiopathic neck pain, prognostic factors, systematic review

Introduction

Musculoskeletal (MSK) conditions pose an enormous burden on individuals, health systems, and social care systems, and are dramatically increasing in developing countries, particularly due to rapidly ageing populations and increasing obesity.¹ Trends of non-fatal diseases show that neck pain is third in the rating of 'years lived with disability' in Europe.² The incidence of neck pain in the general population is estimated between 15–18% per year.^{3,4} In 2016, the prevalence was 20.8 per 1000 patient years in general practitioner practices in the Netherlands.⁵

Most episodes of acute neck pain are thought to resolve with or without treatment. However, Hush et al. found Level 1 evidence that the prognosis of acute idiopathic neck pain is worse than currently recognized.⁶ Childs et al.⁷ suggest that rates of persistent neck pain are substantial: 30% of patients with neck pain will develop chronic symptoms,⁸ and 37% of individuals who experience neck pain will report persistent problems for at least 12 months.³

Chronic pain negatively affects patient perception of general health, interferes considerably with everyday activities as a function of pain severity, is associated with depressive symptoms, and dramatically and negatively affects relationships and interactions with others.⁹ Studies report that the effect of physiotherapy treatment after the occurrence of chronic musculoskeletal pain is at best only moderate.^{10–12} It is therefore essential to prevent chronic pain and ensuing disability in the first place. Knowledge of the clinical course of neck pain and prognostic potentially modifiable and non-modifiable prognostic variables help health care providers to improve clinical decision-making and to manage expectations of people with neck pain.

Prognostic factors are defined as characteristics that are associated with clinical outcomes in patients with a given health condition,¹³ whereas predictive factors are defined as characteristics that identify subgroups of treated patients having different outcomes.¹⁴ Before clinical characteristics can be used to justify specific treatments, it is imperative that the prognostic effects of these characteristics are distinguished from their ability to predict a differential clinical benefit from a specific treatment.¹⁵ Previous research has often used these terms imprecisely.^{16,17} Prior systematic reviews on prognostic factors in nonspecific neck pain have included a majority of studies on patients with whiplash-associated disorder (WAD).^{16–18} The findings of these reviews cannot be generalized to patients with

idiopathic nonspecific, non-traumatic, acute or subacute neck pain because patients with WAD are different in muscle function, cervical pressure pain thresholds, self-reported and patient-specific function, depression, active range of motion, pain intensity and disability in the chronic phase and have different beliefs with regard to recovery.^{19–21} Only one study was found that reported comparable improvement in and prognostic factors for pain, function and recovery between patients with WAD and patients with nonspecific neck pain.²²

Consequently, we think it is essential to analyze the group of nonspecific, acute and subacute neck pain patients separately. Even though Hush et al. did analyze the prognosis of acute idiopathic neck pain, they did not analyze the prognostic factors.⁶ To the best of our knowledge, prognostic factors in this subgroup have not yet been reviewed systematically.

Chronicity has been variously described in three core domains ‘persisting symptoms’, ‘disability’ and ‘work status’.²³ As our primary interest is the prevention of chronic pain, we chose ‘pain intensity’ and ‘perceived non-recovery’ as our outcome variables. This is also in line with the IMPACT recommendations and different observational studies and systematic reviews on chronification of musculoskeletal pain.^{24–28} Besides, in clinical practice patients most often report pain as the most important problem and their treatment aim is to reduce.^{29–31}

The purpose of this study is to identify and synthesize the evidence regarding modifiable and non-modifiable prognostic factors for the development of chronic musculoskeletal neck pain after a first episode of idiopathic, non-traumatic neck pain, operationalized by the outcome variables ‘pain intensity’ and ‘perceived non-recovery’.

Methods

Protocol and registration

We registered the review protocol in the international prospective register of systematic reviews (Prospero) database with registration number CRD42016050346 in October 2016. At that time, there was no other similar review protocol registered on this topic.

This review is written in accordance with Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines.³²

Search

Potentially relevant studies were identified through systematic searches in the following electronic databases: Medline (PubMed), PsycINFO, EMBASE, SPORT-discus and CINAHL. The databases were searched from inception up to October 21, 2017.

A comprehensive search strategy was developed in consultation with a medical information specialist. The search strategy consisted of three major elements: (1) chronification; (2) neck pain; and (3) prognostic factors.

For each element, we collected all known synonyms and related terms to extract the maximum number of articles from the databases. To ensure sufficient precision, the key terms were mapped to medical subject headings (MeSH), and title and abstract search words and phrases were added.

We build the search string for PubMed and then translated it into a syntax for the other databases. All databases were individually searched. We imported all references into RefWorks and excluded duplicate articles. Furthermore, to ensure a maximum number of eligible studies, we scanned the reference lists of all included articles.

The complete search strategy can be found in Appendix 2.1. The translations of the search string to all databases are available on request from the first author.

As a supplement to the systematic search, we also searched the grey literature.

For grey literature we used the following electronic sources up to October 21, 2017: DART-Europe E-theses Portal, Open Access Theses and Dissertations, Networked Digital Library of Theses and Dissertations (NDLTD), ClinicalTrials.gov and WHO International Clinical Trials Registry Platform (ICTRP).

Eligibility criteria

Table 2.1 provides an overview of the in- and exclusion criteria. As we specifically focused on musculoskeletal idiopathic, non-traumatic neck pain, we defined musculoskeletal pain as pain that arises as part of a disease process directly affecting bone(s), joint(s), muscle(s), or related soft tissue(s).³³ Idiopathic, non-traumatic neck pain was defined as neck pain of unknown origin.⁶ We included only studies with a follow-up period of at least 3 months in univariate or multivariate analysis, because chronic pain is defined as pain that persists longer than 3 months or is

recurring.³³ We specifically excluded studies that reported predictive factors for a specific treatment.

Table 2.1: Study selection criteria

Inclusion	Exclusion
Prospective cohort studies	Neck surgery, Radiculopathy and Myelopathy,
Univariate to identify prognostic factors	Headache, wide spread pain, no neck pain at baseline
Human adults (18 years or older) formed at least 60% of the sample*, had to have idiopathic, non-traumatic acute (0–3 weeks) and/or subacute (3–12 weeks) neck pain	Pain not due to musculoskeletal pain (affecting bone(s), joint(s), muscle(s), or related soft tissue(s))
Follow-up period at least 3 months	> 40% of the sample has whiplash related neck pain*
Published in English, Dutch, French or German	
Outcomes pain or perceived non-recovery	

* A threshold of 60% was randomly chosen for pragmatic reasons to not overlook potentially useful prognostic factors.

Study selection

Screening was done by two reviewers (MV and HW) in a two-step procedure. During the first step, the two reviewers independently screened all articles for eligibility based on their title and abstract. During the second step, the same reviewers independently performed a review of the full text articles that were included after the first step. If consensus could not be reached, a third reviewer (FM) made the final decision.

Our final set of studies consisted of all papers for which both reviewers independently decided that they met the inclusion criteria. All disagreements were resolved by discussion.

Data extraction

Two reviewers (MV and HW) independently extracted data from each included study. An extraction manual was designed to facilitate the data collection process. In addition, the reviewers performed a test session to calibrate the extraction process. The following information was collected:

- a) study article (authors, publication date, country),
- b) study design and statistical methods,
- c) characteristics of the study population,
- d) baseline prognostic factors,
- e) primary outcome measurements; i.e. pain intensity, patient perceived

non-recovery, f) time to follow-up, number of patients at follow-up, g) statistical analyses, h) % patients recovered and i) quality of the study.

Risk of bias in individual studies

Risk of bias (RoB) was assessed by two independent reviewers (MV and HW) using the Quality In Prognostic Studies (QUIPS) tool. The QUIPS is a six-item, useful and reliable tool to guide comprehensive assessment of six bias domains in studies of prognostic factors.³⁴ The six domains are study participation, attrition, prognostic factor measurement, outcome measurement, study confounding, and statistical analysis and reporting. The six domains are rated as high, moderate or low RoB. Prior to assessing bias of the included studies, the QUIPS was tested on several non-included studies for calibration purposes. For overall RoB of individual studies, recommendations by Hayden et al.³⁴ were followed, in which a study was considered to be at low RoB when each of the six bias domains was rated as having low RoB. Studies that scored moderate or high RoB on at least one domain were rated as high RoB.³⁴

Synthesis or results

A prognostic factor was defined as a variable that was significantly associated with the main outcomes 'pain intensity' or 'perceived non-recovery'. A significant association was defined as a univariate or multivariate association, or an association adjusted for confounding or other prognostic variables, with a p-value < 0.05, or an Odds Ratio (OR) or Relative Risk with a $\geq 90\%$ CI not including one.³⁵ To be consistent in the direction of the association we calculated the inverse of the Odds Ratios (OR) to determine the OR for non-recovery as four studies used good recovery as their main outcome^{36–39} and two studies used poor recovery as their main outcome.^{40,41}

Meta-analysis was not performed as the included studies were dissimilar with respect to patient population and outcome(s). Therefore, a qualitative data synthesis was performed according to Hayden et al.^{34,42} taking into account the strength and consistency of results (Table 2.2). Following Hayden et al.,^{34,42} a prognostic factor is considered to be of 'limited evidence' if it was researched in only one study. A prognostic factor is considered to be of 'moderate evidence' if more than one high risk of bias study and/or one low risk of bias study provide consistent evidence (> 75% of the studies showing the same direction of effect). 'Strong evidence' is given if more than one low risk of bias study provides consistent evidence.

Table 2.2: Data synthesis^{34,42}

Strong evidence	Consistent findings (defined as > 75% of studies showing the same direction of effect) in multiple low risk of bias studies
Moderate evidence	Consistent findings in multiple high risk of bias and/or one study with low risk of bias
Limited evidence	One study available
Conflicting evidence	Inconsistent findings across studies
No evidence	No association between variables

Two independent reviewers (MV and HW) used a modified GRADE approach⁴³ to judge the overall quality of evidence of all included studies. The approach classifies evidence into high, moderate, low, or very low quality (see Table 2.3), whereby six study characteristics downgrade the quality of evidence (phase of investigation, study limitation, inconsistency, indirectness, imprecision, publication bias), and two study characteristics upgrade the quality of evidence (moderate or large effect size, exposure-response gradient).

Table 2.3: Adapted definitions of the four quality categories according to the original Grading of Recommendations Assessment, Development and Evaluation (GRADE)⁶⁰, applicable to the modified GRADE⁴³

High quality	High confidence that the true effect lies close to that of the estimate of the effect
Moderate quality	Moderate confidence in the effect estimate: the true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different
Low quality	Limited confidence in the effect estimate: the true effect may be substantially different from the estimate of the effect
Very low quality	Very little confidence in the effect estimate: the true effect is likely to be substantially different from the estimate of effect

Results

Study selection

The review selection process is outlined in Figure 2.1. The search strategy resulted in 2,737 articles after removing 1,692 duplicates. After screening titles and abstracts we included 25 articles for detailed full-text screening (see Appendix 2.3). The inspection of all reference lists of these 25 articles and the systematic reviews in

our orientation phase resulted in one additional study for detailed screening. The search in the grey literature resulted in 283 full text articles, none of which met our eligibility criteria.

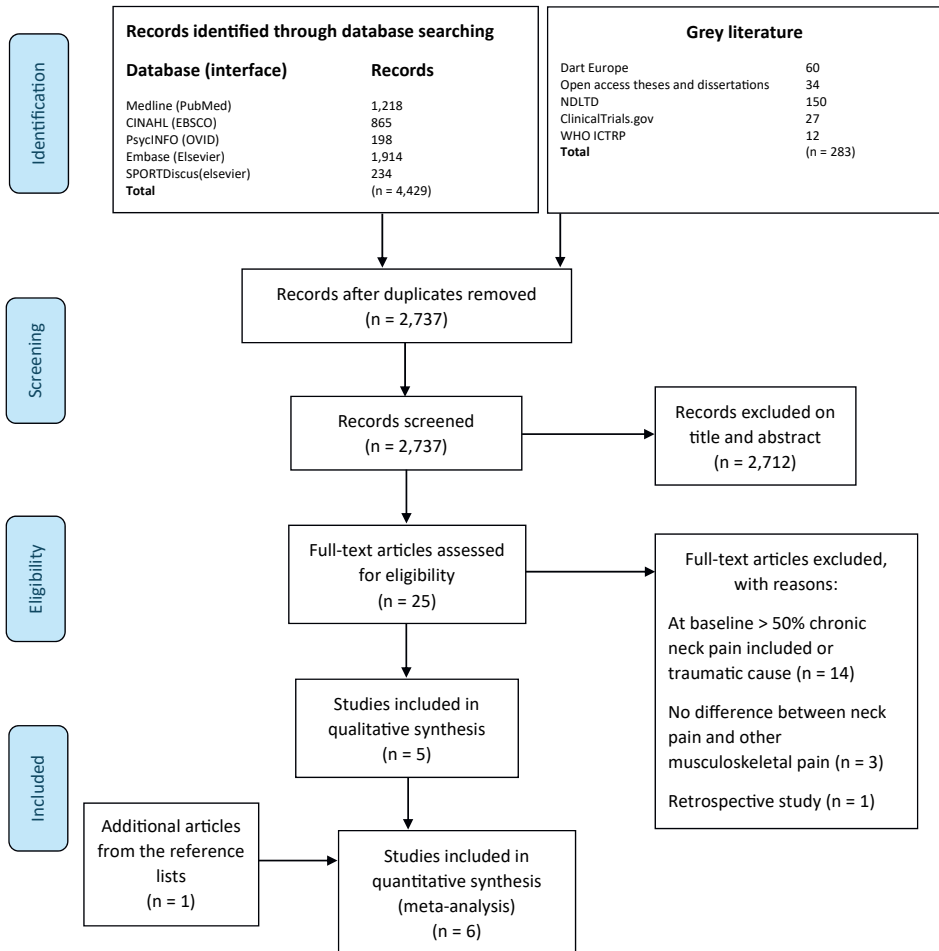


Figure 2.1: PRISMA 2009 flow diagram.

After the detailed full-text screening procedure, our final sample consisted of six articles. Most articles were excluded as they (1) not only analyzed acute and/or subacute idiopathic neck pain patients, but also > 40% traumatic or chronic neck pain patients, or (2) the study did not differentiate between neck pain and other musculoskeletal pain, or (3) the study included healthy participants at baseline. All disagreements were resolved by consensus.

Study characteristics

The characteristics of the six included studies are presented in Appendix 2.2. The six studies^{36–41} were conducted in the Netherlands (four studies),^{36,37,39,40} in the UK (one study)⁴¹ and in Switzerland (one study),³⁸ and analyzed prognostic factors in 2,446 patients with acute and subacute neck pain of which 1,497 (61%) were female and 949 (39%) male.

Of the six studies, four were prospective cohort studies^{37–39,41} and two studies^{36,40} reanalyzed data from randomized controlled (RCTs) trials. One study⁴⁰ included six months follow-up data from two RCTs^{36,37} that were also separately included in this review. As the original RCTs did not report on these data, this study was retained.

Four studies recruited patients from general primary care practices,^{36,37,39,40} one study from chiropractic practices³⁸ and one from the general population.⁴¹

Three^{36,37,41} out of the six studies focused on pain intensity, and five^{36–40} studies on self-perceived non-recovery as the dependent variable. The follow-up periods varied across the included studies. In the three studies that used pain as their main outcome, the follow-up period was three months³⁶ and one year,^{37,41} respectively. Of these three studies, two studies^{36,37} used a NRS pain score (0–10), and in one study⁴¹ the patients were asked whether they had had any ache or pain, which lasted for one day or more (yes/no).

In the studies that used perceived non-recovery as their main outcome, two studies had a follow-up period of three months,^{36,38} one study of six months,⁴⁰ and two studies of one year.^{37,39} Out of the five studies that measured self-perceived non-recovery, three studies used a 7-point Likert scale,^{36,38,39} one study a 6-point Likert scale,³⁷ and one study combined the 6- and 7-point scales.⁴⁰ All scales ranged from ‘completely recovered’ or ‘much improved’ to ‘worse than ever’. Hoving et al.³⁷ and Pool et al.³⁶ defined recovery as ‘completely recovered’ or ‘much improved’, as reported by the patient. Wirth et al.³⁸ defined recovery as “much better” or “better” on their 7-point Likert scale.³⁸ Vos et al.³⁹ analyzed only the group that reported ‘completely recovered’ in their univariate regression analysis. Five studies presented univariate and multivariate analyses. Wirth et al.³⁸ only presented the outcomes of the multivariate analyses.

Risk of bias within studies

The two reviewers agreed 100% on the overall score regarding RoB using the QUIPS tool for all studies. On average there was low RoB in study participation, prognostic factor measurement and outcome measurement. The highest RoB was found in 'study confounding' and 'study attrition' across the six assessed studies. The following Table 2.4 outlines the results of the RoB assessment.

Synthesis of results

We conducted a qualitative data synthesis for both univariate and multivariate results and for each different follow-up period, taking into account the number of studies and their methodological quality.

The included studies analyzed a total of 47 and 43 variables for the outcome variables 'pain intensity' and 'perceived non-recovery', respectively.

At three months follow-up, 18 prognostic factors were investigated for 'pain' as outcome variable. There were no studies at six months for pain, and 34 prognostic factors were investigated in univariate analyses at 12 months follow-up. Multivariate analyses were found in three studies^{36,37,41} with follow up at three or 12 months.

Two studies^{40,41} used poor recovery as their main outcome variable and four studies³⁶⁻³⁹ used good recovery as their main outcome variable. For perceived non-recovery, 18 prognostic factors were investigated in univariate analyses at three months and six months follow-up, and 23 prognostic factors at 12 months follow-up. Multivariate analyses were reported in five studies³⁶⁻⁴⁰ with follow up at three, six or 12 months. However, these studies only reported on the significantly associated variables and not on which factors were included in the primary multivariate analysis.

We present the syntheses of the results for the univariate analysis for the outcome variable 'pain' in Table 2.5 and the outcome variable 'perceived non-recovery' in Table 2.6. The description of the multivariate analyses, for both outcome variables, are presented in Table 2.7. The extensive description and the syntheses of the results can be found in Appendix 2.3 and 2.4.

Table 2.4: Risk of bias QUIPS tool

Studies	Study participation	Study attrition	Prognostic factor measurement	Outcome measurement	Study confounding	Statistical analysis and reporting	Overall score
Hoving et al. ³⁷	Low	Low	Low	Low	High	Low	High
Hill et al. ⁴¹	Low	Moderate	Low	Low	Low	Low	High
Vos et al. ³⁹	Low	Moderate	Low	Low	Moderate	Moderate	High
Pool et al. ³⁶	Moderate	Moderate	Low	Low	High	Moderate	High
Schellingerhout et al. ⁴⁰	Moderate	Low	Low	Low	Moderate	High	High
Wirth et al. ³⁸	Low	High	High	Low	High	Low	High

Pain intensity

In total 47 variables were tested for their prognostic significance (Table 2.5) in three studies; one high RoB study with a follow-up at three months³⁶ and two high RoB studies^{37,41} with a follow-up of 12 months. Only 16 of these 47 variables had a statistically significant association with higher pain, while two of the 47 variables had a statistically significant association with decreased pain.

Based on the univariate and multivariate analysis^{36–41} we found *moderate evidence* for ‘age > 40 years’ and ‘concomitant back pain’ to be prognostic for ‘pain intensity’ at 12 months follow-up.

Two high RoB studies found these variables to be significant in these analyses.

Based on the univariate analyses we found *conflicting evidence* for the variables ‘female gender’ and ‘neck injury/traumatic cause’ at 12 months follow-up.^{37,41}

Table 2.5: Univariate level of evidence of positive association with a higher pain intensity

Prognostic factors	3 months	12 months
Social demographic		
Age ≥ 40 years		+
Age 18–29 years (ref)		
30–44 years		+
45–59 years		+*
60–75 years		+*
Age (in years)	+	
Gender (female)	+*	+/-
Social class		
Nonmanual (ref)		
Manual		+
Marital status		
Married/partner (ref)		
Other		+
Children		
None (ref)		
1		-
2		+
≥ 3		+
Nonworking		+*
Symptoms		
Low Back Pain		+*
Pain intensity at baseline	+	+*

Table 2.5 continues on next page.

Table 2.5: Continued

Prognostic factors	3 months	12 months
Severity of complaints	+	
Duration of the neck pain		
2–6 weeks (ref)		
7–12 weeks		+
≥ 13 weeks		+
Radiating pain below elbow		+
Headache (of cervical origin)		+
No change in neck pain previous 2 weeks		+
Distributed sleep due to neck pain		+
High severity of physical dysfunctioning		+
GCPs (grade)		
1 = low intensity (ref)		
2 = high intensity	-	
3 = moderately limiting	-	
4 = severity limiting	-	
Prior conditions / cause problem		
Previous episodes of neck pain	+	+
Neck injury / traumatic cause		+/-
Physical activities		
Standing/walking in last job ≥ 2 hours		+
Driving in last job ≥ 4 hours		-
Digging/shoveling in last job		-
Sitting in last job ≥ 2 hours		-
Lifting in last job ≥ 25 lb weights		+
Gardening at last once or twice a week		+
Do-it-yourself work often		+
Walking each day ≥ 30 min		+
Cycling each day		+
TV hours > 3 hours per day		-
Physical activity last than average		+
Psychological factors		
Catastrophizing (PCCL)	+	
Coping (PCCL)	+	
Internal pain control (PCCL)	-	
External pain control (PCCL)	+	
TSK (higher score)	+	
Somatization (4DSQ)	+	
Fear (4DSQ)	+	
Distress (4DSQ)	+	
Depression (4DSQ)	+	
Job satisfaction		+
Satisfaction at not working		+

Table 2.5 continues on next page.

Table 2.5: Continued

Prognostic factors	3 months	12 months
General health		
BMI		
< 22.5 (ref)		
22.5–25.0		+
25.1–27.4		+
≥ 27.5		+
Smoking status		
Never (ref)		
Past		+
Current		+
Alcohol intake		
< 3 days per week (ref)		
> 3 days per week		–*
Perceived General Health		
Excellent (ref)		
Good		+
Fair		+
Poor		+*
GHQ		
< 8 (ref)		
8–11		+*
12–17		+
≥ 18 poor psychological health		+*
Remaining factors		
Patients preference		
None (ref)		
Pt	–	
Mt	–	
GP attitude		
Purely biomedical (ref)		
More biomedical	–	
Neutral	–	

+ = Positive association of prognostic factor with perceived non-recovery.

– = Negative association of prognostic factor with perceived non-recovery.

* = Significant prognostic value.

GCPS = Graded Chronic Pain Scale, GHQ = general health questionnaire, GP = General Practitioner, PCCL = Pain Coping and Cognition list, TSK = Tampa Scale of Kinesiophobia, 4DSQ = Four Dimension Psychological Symptomatology Questionnaire.

Strong	Moderate	Limited	Conflicting	No evidence
--------	----------	---------	-------------	-------------

As each of in total 16 variables was only measured in one study,^{36,37,41} we considered these variables as having *limited evidence* for an association with higher pain. Five of these 18 variables were measured at three months, and 11 variables at 12 months.

In multivariate analyses (Table 2.6) only older age and concomitant LBP were retained in the model in more than one study, confirming *moderate evidence* for these variables. Distress was retained as a significant prognostic variable in the multivariate analyses at 12 months in one study with high RoB, which was considered as *limited evidence*.³⁶

Perceived non-recovery

Perceived non-recovery was measured in five studies at three,^{36,38} six,⁴⁰ and twelve^{37,39,41} months follow-up. In total, 43 variables were tested on their prognostic value (Table 2.6).

We found *moderate evidence* for a 'previous period of neck pain' and 'accompanying headache' at 12 months. The results of Vos et al.³⁹ showed a significant association with non-recovery, Hoving et al.³⁷ showed the similar results, however the association was non-significant. We therefore considered this as moderate evidence.

We found *limited evidence* for 'accompanying headache' and an 'increased fear of movement (TSK)' for perceived non-recovery and 'female gender' for perceived non-recovery at three months. At six months follow-up limited evidence was found for 10 variables.⁴⁰ With regard to one-year follow-up, nine variables in one study had a statistically significant association with perceived non-recovery and were considered as limited evidence.^{37,39,41} One factor (GP advice to wait and see) had a positive impact on recovery.³⁹

In one multivariate analysis, depression was not retained as a significant prognostic factor at three months,³⁶ but was retained in another study (Table 2.7).³⁸ At six months seven variables were found to be significantly associated with non-recovery.⁴⁰ Three studies tested prognostic factors at 12 months in a multivariate analysis.^{36,37,39} No common factor across the three studies was identified that was significantly associated with persistent complaints defined as non-recovery.

Based on the analysis of the multivariable models we found no prognostic factor that was retained as significant in more than one model (Table 2.7). This does not lend support for the evidence of some prognostic factors found in the univariate analyses.

Table 2.6: Univariate level of evidence of positive association with perceived non-recovery

Prognostic factors	3 months	6 months	12 months
Social demographic			
Age ≥ 40 years	+		+
Age (in years)	+	-*	
Age-square		+	
Gender (female)	+	-	+*/-
Level of education			
High (ref)			
Middle		+	
Low		+	
Employment status (yes = 1)		-	
Symptoms			
Low back pain		+	+
Severe initial pain	+	-	+
Severe initial pain square		+	
Severity of complaints	-		
Duration of complaints > 2 weeks			+
Duration current episode			
1–3 months		-	+
> 3 months		-	+
Pain in the upper part of the neck			+
Accompanying headache	+	+	+
Radiating pain below elbow			+
Radiating to the back			+
Radiating pain (yes = 1)		-*	
No change in neck pain previous 2 weeks			+
Disturbed sleep due to neck pain			-
Accompanying dizziness (yes = 1)		+	
High severity of physical dysfunction			+
GCPS (grade)			
1 = low intensity (ref)			
2 = high intensity	-		
3 = moderately limiting	+		
4 = severely limiting	-		
Total score on the NDI (higher score)		+	+
Total score on the ALBPSQ			+
Prior conditions/ cause problem			
Previous episodes of neck pain	+	+	+
Traumatic cause		+	+
Psychological factors			
Catastrophizing (PCCL)	+		
Coping (PCCL)	-		
Internal pain control (PCCL)	-		

Table 2.6 continues on next page.

Table 2.6: Continued

Prognostic factors	3 months	6 months	12 months
External pain control (PCCL)	-		
TSK (higher score)	+*	+*	
Somatization	+		
Fear (4DSQ)	+		
Distress (4DSQ)	+		
Depression (4DSQ)	+*		
General health			
EuroQOL VAS		+*	
Remaining factors			
Patients preference			
None (ref)			
Pt	-	-	
Mt	-	+	
GP attitude			
Purely biomedical (ref)			
More biomedical	+		
Neutral	-		
Treated for neck pain in the past (yes = 1)		+*	
Treated by physiotherapist before			+*
Treated by manual therapist before			+*
GP advised to wait and see			-*
GP advised to improve posture			-
GP prescribed medication			+
GP instructed in physical exercises			-

+ = Positive association of prognostic factor with perceived non-recovery.

- = Negative association of prognostic factor with perceived non-recovery.

* = Significant prognostic value.

ALBPSQ = Acute Low Back Pain Screening Questionnaire, EuroQOL = quality of Life Scale, GCPS = Graded Chronic Pain Scale, GP = General Practioner, NDI = Neck Disability Index, PCCL = Pain Coping and Cognition list, TSK = Tampa Scale of Kinesiophobia, 4DSQ = Four Dimension Psychological Symptomatology Questionnaire.

Strong	Moderate	Limited	Conflicting	No evidence
--------	----------	---------	-------------	-------------

Table 2.7: Summary of the multivariable models

Prognostic factors for a positive association with pain			
Author	3 months	12 months	Explained variance / discriminative ability model
Pool et al. ³⁶	Gender (male) OR 3.13 (1.5–6.67) Less severity of complaints OR 0.74 (0.57–0.95) Fear of movement (TSK) OR 1.09 (1.02–1.15)	Distress (4DSQ) (not given)	R ² explained variance 16% for non-recovery of pain at 3 months. R ² Explained variance at 12 months not given.
Hoving et al. ³⁷		> 40 year β 1.11 (0.38–1.84) Low back pain β 0.80 (–0.02–1.61) Duration of the neck pain $\geq$ 13 weeks β 1.35 (0.34–1.93) Previous episodes of neck pain β 1.35 (0.13–1.58) Pain intensity at baseline β 0.26 (0.07–0.45)	R ² explained variance 30% for non-recovery of pain at 12 months.
Hill et al. ⁴¹		45–59 years OR 3.9 (2.2–6.7) Low back pain OR 1.6 (1.1–2.2) Nonworking OR 1.6 (1.1–2.3) Cycling each day OR 2.4 (1.5–4.0)	R ² explained variance not given
Prognostic factors for perceived non-recovery			
Author	3 months	6 months	12 months
Pool et al. ³⁶	Accompanying headache OR 3.70 (1.47–9.09) <i>Patient preference physiotherapy</i> OR 0.22 (0.05–1.03)		Fear of movements (TSK) ³⁶ (not given)
			R ² explained variance 17% for perceived non-recovery at 3 months. R ² explained variance at 12 months not given.

Table 2.7 continues on next page.

Table 2.7: Continued

Prognostic factors for perceived non-recovery				Explained variance / discriminative ability model
Author	3 months	6 months	12 months	
Hoving et al. ³⁷			>40 year OR 3.85 (1.64–9.09) Concomitant LBP OR 2.7 (1.25–5.88) No change in neck pain previous 2 weeks OR 3.03 (1.52–5.88) Traumatic cause OR 2.5 (0.95–6.67) High severity of physical dysfunction OR 1.85 (0.90–3.7)	R ² explained variance not given.
Vos et al. ³⁹			Female gender OR 4.55 (1.39–14.29) Pain in the upper part of the neck OR 1.85 (1.32–2.56) Duration of complaints > 2 weeks OR 3.03 (1.10–8.33) Pain radiating to the back OR 1.89 (1.23–2.86) GP advised to wait and see OR 0.15 (0.03–0.63)	R ² explained variance 38% for perceived non- recovery at 12 months.

Schellingerhout et al. ⁴⁰	Age OR 1.03 (1.01–1.05) Previous episode of neck pain OR 1.67 (1.25–2.24) Trauma as cause of the complaints OR 1.26 (1.02–1.56) Concomitant LBP OR 2.29 (1.27–4.12) Paid employment OR 1.45 (1.03–2.05) Accompanying headache * pain intensity OR 1.12 (1.01–1.24) Accompanying headache * radiation pain OR 1.48 (1.03–2.12) <i>Radiation of pain to elbow/shoulder OR 0.57 (0.42–0.77)</i> <i>Accompanying headache * previous neck complaints OR 0.69 (0.48–0.98)</i> <i>Accompanying headache * employment status OR 0.44 (0.30–0.65)</i>	Discriminative ability 0.66 (95% CI 0.61–0.71). A confidence interval of 84.3% corresponds with their criterion ($P < 0.157$). Multivariable model tested in independent cohort: Discriminative ability (AUC) of 0.66 (95% CI 0.59–0.72)
Wirth et al. ³⁸	Depression BQ 1.30 (1.02–1.64) Age 1.03 (0.98–1.09) Pain at baseline 1.14 (0.76–1.67)	Nagelkerke $R^2 = 0.21$; AUC = 0.80 (95% CI 0.69–0.91; $P = 0.002$)

OR = Odds Ratio > 1 positive association, < 1 negative association with non-recovery.^{36–41} β = Regression coefficient, 95% CI > 0 bad / < 0 good for pain intensity.³⁷ Variables with a statistically prognostic value of a lower probability of persistent complaints shown in red. TSK = Tampa Scale of Kinesiophobia. 4DSQ = Four Dimension Psychological Symptomatology Questionnaire, BQ = Bournemouth Questionnaire. Prognostic factors with a negative association with pain or perceived non-recovery shown in italics. Prognostic factors who retained in 2 multivariable models shown in bold.

Quality of evidence

We present the assessment of the modified GRADE in Appendix 2.5 and 2.6. We included 5 primary studies (phase 1) and one explanatory study (phase 3). The quality of evidence was downgraded for all prognostic factors researched in the primary studies. We also downgraded all prognostic factors on 'study limitation' due to the high risk of bias assessed with the QUIPS tool (Table 2.4). 'Publication bias', 'imprecision' and 'inconsistency' were for most of the prognostic factors not applicable due to the limited number of included studies, resulting in a limitation (down) grading. When a prognostic factor showed consistent evidence over different follow-up periods, 'inconsistency' was graded as no serious limitation. No serious limitations for 'imprecision' were graded when there were 2 included studies on one prognostic factor, large enough sample sizes and no intervals reported in both no effect and appreciable risk and protective values. There were no serious limitations on 'indirectness'. We could only increase the quality of evidence for moderate effect size for a few prognostic factors with an OR of > 2.5. For the outcome variable pain intensity we found only low quality evidence for the prognostic factor 'older age'. For the outcome variable perceived-recovery we found only low quality evidence for 'older age' and 'accompanying headache', and low back pain, a previous episode of neck pain and a higher score on the TSK at 6 months. For the other prognostic factors we had to downgrade the quality of evidence to very low.

Discussion

We systematically synthesized the evidence of prognostic factors for the development of chronic musculoskeletal neck pain or perceived non-recovery after a first episode of idiopathic, non-traumatic neck pain. We found moderate evidence for 'age > 40 years' and 'concomitant back pain' to be prognostic for 'pain intensity'. For the outcome 'perceived non-recovery', we found moderate evidence for both 'a previous period of neck pain' and 'accompanying headache'.

However, we found only low or very low quality evidence for these prognostic factors.

Other studies found similar prognostic factors in musculoskeletal problems.^{35,44–46} Concomitant headache and low back pain (LBP) were found to be prognostic for 'chronicity' after an acute whiplash injury⁴⁶ and for 'time to recover' from a new

episode of idiopathic neck pain.⁴⁷ A previous episode of pain has been reported as a generic prognostic factor for musculoskeletal pain^{35,45} and chronic WAD.⁴⁶ Were Mallen et al.⁴⁵ and Leaver et al.⁴⁷ found 'older age' of prognostic value.

Posttraumatic stress symptoms, passive coping and high catastrophizing are prognostic factors for chronification of WAD.^{46,48} Avoidance beliefs, catastrophizing, depressive symptoms and distress were found to be prognostic factors for chronification of LBP.^{49–52} The literature found similar psychological problems (e.g. psychological stress, anxiety, fear-avoidance beliefs and catastrophizing) associated with chronic idiopathic, non-traumatic neck pain.^{53–55} It is therefore surprising that in prognostic studies on the persistence of acute idiopathic neck pain so very few of these modifiable psychological variables were researched. Only one study³⁶ included a number of relevant psychological variables on both outcome variables at 3 months. Hill et al.⁴¹ measured two psychological variables for the outcome variable pain at 12 months, whereas Schellingerhout et al.⁴⁰ and Wirth et al.³⁸ measured 'kinesiophobia' and 'depression', respectively, as a modifiable variable at 6 and 3 months, respectively, on perceived non-recovery.

We assessed study quality with the QUIPS-tool. The QUIPS-tool considers an overall high RoB when only one of the six-domains is of moderate or high RoB. We are well aware that the QUIPS-tool does not make any difference in degree of bias and is thereby strict in its conclusions. However, the overall high RoB is comparable with other systematic reviews that have included the same studies.^{16,17}

Strengths and limitations

Our study contributes to the literature by identifying prognostic factors for chronicity in patients with idiopathic, non-traumatic acute and/or subacute neck pain. We do so by only reviewing studies of which at least 60% of the population consisted of these patients. Ideally, all studies that included patients with chronic neck pain and/ or with a traumatic cause would be excluded from the review. However, this would have resulted in an even much lower number of studies making it impossible to synthesize any evidence. We only found six studies, five of which were phase 1 explanatory studies. For example, the study of Schellingerhout et al.⁴⁰ included data from one RCT on chronic neck pain (34% of subjects), which explains why variables such as 'duration of complaints ≥ 13 weeks' and 'traumatic cause' were included in this review.

Consequently, one cannot consider these variables as prognostic factors for the group of patients with idiopathic, acute and subacute neck pain although they could have influenced the outcomes of these specific studies.^{37,40,41}

A strength of our study is that we did not only judge the level of evidence, but that we also critically assessed the quality of our findings. This allowed to distinguish between level and quality of evidence, and hence, for a more reliable assessment of the results of existing studies.

The results found in our systematic review have to be interpreted with caution. A first point of attention is that Vos et al.³⁹ used a CI of 90% in their univariate analysis whereas the other five studies^{36–38,40,41} used a CI of 95%. In the multivariate analysis five studies^{36–39,41} used a 95% CI; Schellingerhout et al.,⁴⁰ however, used a CI of 84.3%. By using a smaller confidence interval the chance that type 1 errors occurs increases.⁵⁶

Second, we included studies that used data from randomized clinical trials.^{36,37,40} It is questionable whether data from randomized clinical trials are appropriate to identify modifiable variables for persistent pain or non-recovery. The applied therapy could have affected the found associations: if the therapy is effective, these patients will experience less or no pain, and the effect of the prognostic factors is mitigated. The effect of treatment can be seen as an effect modifier.⁵⁷ Prognostic factors could be at best researched in the non-treatment or placebo arm of RCT's,¹⁴ instead of adjusting for intervention in regression analysis.

Third, there is still some uncertainty about the exact sample composition and the analyzed factors in the study from Schellingerhout et al.⁴⁰ as this study pooled data from three other studies.^{36,37,58} These three studies, however, analyzed different factors and also used different selection criteria for their cohorts. Combining these studies therefore resulted in large amounts of missing data for some of the variables. It is not clear how the authors dealt with missing data. We therefore have to interpret these findings with caution.

Fourth, despite the fact that the included studies used a similar tool for measuring perceived recovery, they interpreted it differently in their data analyses. While Vos et al.³⁹ analyzed only the group who was 'completely recovered' as recovered, Hoving et al.³⁷ and Pool et al.³⁶ also included the group who were 'much improved'. Wirth et al.³⁸ considered 'much better' and 'better' as recovered. Based on these different interpretations, it can be questioned whether the results for this outcome

variable can be compared. In addition, the prognostic variables have to be well described and measured with valid tools. The included studies used different tools for measuring the same construct, for instance depression.^{36,38} Additionally, the interpretation of some variables is unclear. Pool et al.³⁶ measured 'pain at inception' and 'severity of complaints' at baseline. It is unclear whether practitioners and patients can differentiate between the two.

We therefore recommend to develop a Core Outcome Set for neck pain and the use of consistent measurements and definitions for the dependent and independent variables in further research. Only then is it possible to obtain valuable evidence and useful data for practice.

Another limitation of our study could be that we did not include secondary measures, such as pain related disability. However, it is known that pain and disability are distinct constructs as not every person with persistent pain also experiences disability.⁵⁹ Nevertheless from a clinical and health perspective neck-related disability and work status are important outcomes, and further research should measure pain intensity, disability and work status as distinct dimensions of persistent pain. However, identifying prognostic factors for disability and work status was beyond the scope of this review.

Further research

The focus in health care must be on the prevention of chronic pain. As mentioned above, chronic neck pain influences not only quality of life, but also impacts health care costs worldwide. Prevention is therefore key in combatting this, and opportunities for the prevention of chronicity only exist in acute and subacute patients.

Given that we found no low RoB study, and because of the specific limitations as outlined above, there is much need for a conclusive and comprehensive cohort study on prognostic factors for chronification of acute or subacute idiopathic, non-traumatic, neck pain. Special attention must be given to modifiable prognostic factors.

Conclusion

We have identified moderate and limited evidence to support the presence of a number of prognostic factors in patients with acute or subacute musculoskeletal,

non-traumatic neck pain that are associated with pain or perceived non-recovery up until one year after onset of pain.

Such factors include higher age (> 40 years), concomitant LBP or headache and a previous period of neck pain. Nevertheless, the quality of this evidence is graded as low to very low. Further research is needed before drawing definite conclusions about the prognostic value of these factors.

Funding

This research was supported by the Institute of Movement studies. We did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Acknowledgements

The authors thank Jurgen Mollema, Utrecht University of Applied Sciences, for the assistance with the search strategy, and Cas Kruitwagen, Utrecht University, for the helpful comments on the statistical analysis.

References

1. Hoy D, Geere J-A, Davatchi F, Meggitt B, Barrero LH. A time for action: Opportunities for preventing the growing burden and disability from musculoskeletal conditions in low- and middle-income countries. *Best Pract Res Clin Rheumatol*. 2014;28(3):377–93. doi:10.1016/j.berh.2014.07.006.
2. GBD 2015 Disease and Injury Incidence and Prevalence Collaborators G 2015 D and II and P. Global, regional, and national incidence, prevalence, and years lived with disability for 310 diseases and injuries, 1990–2015: a systematic analysis for the Global Burden of Disease Study 2015. *Lancet* (London, England). 2016;388(10053):1545–602. doi:10.1016/S0140-6736(16)31678-6.
3. Côté P, Cassidy DJ, Carroll LJ, Kristman V. The annual incidence and course of neck pain in the general population: a population-based cohort study. *Pain*. 2004;112(3):267–73. doi:10.1016/j.pain.2004.09.004.
4. Croft PR, Lewis M, Papageorgiou AC, et al. Risk factors for neck pain: a longitudinal study in the general population. *Pain*. 2001;93(3):317–25.
5. Koppes D. Zorg voor de fysiotherapeut - top-10 gezondheidsproblemen (DCSPH). Nivel. <http://www.nivel.nl/node/4677>.
6. Hush JM, Lin CC, Michaleff ZA, Verhagen A, Refshauge KM. Prognosis of Acute Idiopathic Neck Pain is Poor: A Systematic Review and Meta-Analysis. *YAPMR*. 2011;92: 824–29. doi:10.1016/j.apmr.2010.12.025.
7. Childs JD, Cleland JA, Elliott JM, et al. Neck Pain: Clinical practice guidelines linked to the international classification of functioning, disability, and health from the orthopedic section of the american physical therapy association. *J Orthop Sport Phys Ther*. 2008;38(9):A1–A34. doi:10.2519/jospt.2008.0303.
8. Bovim G, Schrader H, Sand T. Neck pain in the general population. *Spine* (Phila Pa 1976). 1994;19(12):1307–9. doi:10.1097/00007632-199406000-00001.
9. Reid KJ, Harker J, Bala MM, et al. Epidemiology of chronic non-cancer pain in Europe: narrative review of prevalence, pain treatments and pain impact. *Curr Med Res Opin*. 2011;27(2):449–62. doi:10.1185/03007995.2010.545813.
10. Geneen LJ SB, Andrew Moore R, Clarke C, Martin D, Colvin LA, Smith BH. Cochrane Database of Systematic Reviews Physical activity and exercise for chronic pain in adults: an overview of Cochrane Reviews (Review) Physical activity and exercise for chronic pain in adults: an overview of Cochrane Reviews (Review) i Physical acti. *Cochrane Database Syst Rev*. 2017;(4). doi:10.1002/14651858.CD011279.pub3.
11. Bertozzi L, Gardenghi I, Turoni F, et al. Effect of Therapeutic Exercise on Pain and Disability in the Management of Chronic Nonspecific Neck Pain: Systematic Review and Meta-Analysis of Randomized Trials. *Phys Ther*. 2013;93(8):1026–36.
12. Gross A, Langevin P, Burnie SJ, et al. Manipulation and mobilisation for neck pain contrasted against an inactive control or another active treatment. *Cochrane Database Syst Rev*. 2015;23(9). doi:10.1002/14651858.CD004249.pub4.
13. Riley RD, Hayden JA, Steyerberg EW, et al. Guidelines and Guidance Prognosis Research Strategy (PROGRESS) 2: Prognostic Factor Research. *PLOS Med*. 2013;10(2):e1001380. doi:10.1371/journal.pmed.1001380.
14. Adolffson J, Steineck G. Prognostic and treatment-predictive factors – is there a difference? *Nature*. 2000;3:265–8.

15. Clark GM. Prognostic factors versus predictive factors: Examples from a clinical trial of erlotinib. *Mol Oncol*. 2008;1:406–12. doi:10.1016/j.molonc.2007.12.001.
16. Wingbermühle RW, van Trijffel E, Nelissen PM, Koes B, Verhagen AP. Few promising multivariable prognostic models exist for recovery of people with non-specific neck pain in musculoskeletal primary care: a systematic review. *J Physiother*. 2018;64(1):16–23. doi:10.1016/j.jphys.2017.11.013.
17. Kelly J, Ritchie C, Sterling M. Clinical prediction rules for prognosis and treatment prescription in neck pain: A systematic review. *Musculoskelet Sci Pract*. 2017;27:155–164. doi:10.1016/j.math.2016.10.066.
18. Walton DM. 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(1):494–505. doi:10.2174/1874325001307010494.
19. Stenneberg MS, Rood M, de Bie R, Schmitt MA, Cattrysse E, Scholten-Peeters GG. To What Degree Does Active Cervical Range of Motion Differ Between Patients With Neck Pain, Patients With Whiplash, and Those Without Neck Pain? A Systematic Review and Meta-Analysis. *Arch Phys Med Rehabil*. 2017;98(7):1407–34. doi:10.1016/j.apmr.2016.10.003.
20. Anstey R, Kongsted A, Kamper S, Hancock MJ. Are People With Whiplash-Associated Neck Pain Different From People With Nonspecific Neck Pain? *J Orthop Sport Phys Ther*. 2016;46(10):894–901. doi:10.2519/jospt.2016.6588.
21. Ris I, Juul-Kristensen B, Boyle E, Kongsted A, Manniche C, Søgaard K. Chronic neck pain patients with traumatic or non-traumatic onset: Differences in characteristics. A cross-sectional study. *Scand J Pain*. 2017;14:1–8. doi:10.1016/j.sjpain.2016.08.008.
22. Verhagen AP, Lewis M, Schellingerhout JM, et al. Do whiplash patients differ from other patients with non-specific neck pain regarding pain, function or prognosis? *Man Ther*. 2011;16(5):456–62. doi:10.1016/j.math.2011.02.009.
23. Pincus T, Kim Burton A, Vogel S, Field AP. A Systematic Review of Psychological Factors as Predictors of Chronicity/Disability in Prospective Cohorts of Low Back Pain. *Spine (Phila Pa 1976)*. 2002;27(5):E109–20.
24. Gewandter JS, Dworkin RH, Turk DC, et al. Research design considerations for chronic pain prevention clinical trials: IMMPACT recommendations HHS Public Access. *Pain*. 2015;156(7):1184–97. doi:10.1097/j.pain.0000000000000191.
25. Pierik J, IJzerman M, Gaakeer M, et al. Incidence and prognostic factors of chronic pain after isolated musculoskeletal extremity injury. *Eur J Pain*. 2016;20(5):711–22. doi:10.1002/ejp.796
26. Bérubé M, Gélinas C, Choinière M, et al. The effect of psychological interventions on the prevention of chronic pain in adults: A systematic review protocol. *Syst Rev*. 2017;6(1):190. doi:10.1186/s13643-017-0583-7
27. Traeger AC, Henschke N, Hübscher M, et al. Estimating the Risk of Chronic Pain: Development and Validation of a Prognostic Model (PICKUP) for Patients with Acute Low Back Pain. *PLoS Med*. 2016;13(5):e1002019. doi: 10.1371/journal.pmed.1002019
28. Struyf F b, Geraets J., Noten S. b, Meeus M. b d, Nijs J. e f. A multivariable prediction model for the chronification of non-traumatic shoulder pain: A systematic review. *Pain Physician*. 2016;19(2):1–10. doi:10.1017/CBO9781107415324.004.

29. Sanderson T, Morris M, Calnan M, Richards P, Hewlett S. UKPMC Funders Group Patient perspective of measuring treatment efficacy : the Rheumatoid Arthritis Patient Priorities for Pharmacological Interventions (RAPP-PI) outcomes. *Arthritis Rheum.* 2010;62(5):647–56. doi:10.1002/acr.20151.Patient.
30. Casarett D, Karlawish J, Sankar P. Designing pain research from the patient's perspective: what trial end points are important to patients with chronic pain? *Pain Med.* 2001;2(4):309–16. doi:10.1046/j.1526-4637.2001.01041.x
31. Bromley Milton M, Börsbo B, Rovner G, Lundgren-Nilsson Å, Stibrant-Sunnerhagen K, Gerdle B. Is Pain Intensity Really That Important to Assess in Chronic Pain Patients? A Study Based on the Swedish Quality Registry for Pain Rehabilitation (SQRP). *PLoS One.* 2013;8(6). doi:10.1371/journal.pone.0065483.
32. Moher D, Liberati A, Tetzlaff J, Altman DG, PRISMA Group T. Preferred Reporting Items for Systematic Reviews and Meta-Analyses: The PRISMA Statement. *J Clin Epidemiol.* 2009;62:1006–12. doi:10.1016/j.jclinepi.2009.06.005.
33. Treede R-D, Rief W, Barke A, et al. A classification of chronic pain for ICD-11. *Pain.* 2015;156(6):1003–7. doi:10.1097/j.pain.0000000000000160.
34. Hayden JA, van der Windt DA, Cartwright JL, Côté P, Bombardier C. Assessing Bias in Studies of Prognostic Factors. *Ann Intern Med.* 2013;158(4):280. doi:10.7326/0003-4819-158-4-201302190-00009.
35. Artus M, Campbell P, Mallen CD, Dunn KM, Van Der Windt DAW. Generic prognostic factors for musculoskeletal pain in primary care: a systematic review. *BMJ Open.* 2017;7. doi:10.1136/.
36. Pool JJM, Ostelo RWJG, Knol D, Bouter LM, De Vet HCW. Are psychological factors prognostic indicators of outcome in patients with sub-acute neck pain? *Man Ther.* 2010;15:111–6. doi:10.1016/j.math.2009.08.001.
37. Hoving JL, De Vet HCW, Twisk JWR, et al. Prognostic factors for neck pain in general practice. *Pain.* 2004;110:639–45. doi:10.1016/j.pain.2004.05.002.
38. Wirth B, Humphreys BK, Peterson C. Importance of psychological factors for the recovery from a first episode of acute non-specific neck pain - a longitudinal observational study. *Chiropr Man Therap.* 2016;24(9). doi:10.1186/s12998-016-0090-2.
39. Vos CJ, Verhagen AP, Passchier J, Koes BW. Clinical course and prognostic factors in acute neck pain: An inception cohort study in general practice. *Pain Med.* 2008;9(5):572–580. doi:10.1111/j.1526-4637.2008.00456.x.
40. 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):827–35. doi:10.1097/BRS.0b013e3181d85ad5
41. 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):1648–54. doi:10.1097/01.BRS.0000132307.06321.3C.
42. Hayden JA, Tougas ME, Riley R, Iles R, Pincus T. Individual recovery expectations and prognosis of outcomes in non-specific low back pain: Prognostic factor exemplar review. *Cochrane Database Syst Rev.* 2014. doi:10.1002/14651858.CD011284.
43. Huguet A, Hayden JA, Stinson J, et al. Judging the quality of evidence in reviews of prognostic factor research: adapting the GRADE framework. *Syst Rev.* 2013;2(1):1. doi:10.1186/2046-4053-2-71.

44. Bier JD, Ostelo RWJG, van Hooff ML, Koes BW, Verhagen AP. Validity and Reproducibility of the STarT Back Tool (Dutch Version) in Patients With Low Back Pain in Primary Care Settings. *Phys Ther*. 2017;97(5):561–70. doi:10.1093/ptj/pzx023.
45. Mallen CD, Peat G, Thomas E, Dunn KM, Croft PR. Prognostic factors for musculoskeletal pain in primary care: a systematic review. *Br J Gen Pract*. 2007;57(541):655–61.
46. 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 Sport Phys Ther*. 2013;43(2):31–43. doi:10.2519/jospt.2013.4507.
47. Leaver AM, Maher CG, McAuley JH, Jull G, Latimer J, Refshauge KM. People seeking treatment for a new episode of neck pain typically have rapid improvement in symptoms: An observational study. *J Physiother*. 2013;59(1):31–7. doi:10.1016/S1836-9553(13)70144-9.
48. Campbell L, Smith A, McGregor L, Sterling M. Psychological Factors and the Development of Chronic Whiplash Associated Disorder(s). *Clin J Pain*. 2018;34(8):1. doi:10.1097/AJP.0000000000000597.
49. Wertli MM, Rasmussen-Barr E, Weiser S, Bachmann LM, Brunner F. The role of fear avoidance beliefs as a prognostic factor for outcome in patients with nonspecific low back pain: A systematic review. *Spine J*. 2014;14(5):816–36. doi:10.1016/j.spinee.2013.09.036.
50. Wertli MM, Eugster R, Held U, Steurer J, Kofmehl R, Weiser S. Catastrophizing - A prognostic factor for outcome in patients with low back pain: A systematic review. *Spine J*. 2014;14(11):2639–57. doi:10.1016/j.spinee.2014.03.003.
51. George SZ, Beneciuk JM. Psychological predictors of recovery from low back pain: A prospective study. *BMC Musculoskelet Disord*. 2015;16(1):1–7. doi:10.1186/s12891-015-0509-2.
52. Nicholas MK, Linton SJ, Watson PJ, Main CJ. Early Identification and Management of Psychological Risk Factors (“Yellow Flags”) in Patients With Low Back Pain: A Reappraisal. *Phys Ther*. 2011;91(5):737–53. doi:10.2522/ptj.20100224.
53. Ortego G, Villafañe JH, Doménech-García V, Berjano P, Bertozzi L, Herrero P. Is there a relationship between psychological stress or anxiety and chronic nonspecific neck-arm pain in adults? A systematic review and meta-analysis. *J Psychosom Res*. 2016;90:70–81. doi:10.1016/j.jpsychores.2016.09.006.
54. Thompson DP, Urmston M, Oldham JA, Woby SR. The association between cognitive factors, pain and disability in patients with idiopathic chronic neck pain. *Disabil Rehabil*. 2010;32(21):1758–67. doi:10.3109/09638281003734342.
55. 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):239–48. doi:10.1016/j.math.2007.01.010.
56. Akobeng AK. Understanding type I and type II errors, statistical power and sample size. *Acta Paediatr*. 2016;105(6):605–9. doi:10.1111/apa.13384.
57. Hancock M, Herbert RD, Maher CG. A Guide to Interpretation of Studies Investigating Subgroups of Responders to Physical Therapy Interventions. *Phys Ther*. 2009;89(7):698–704. doi:10.2522/ptj.20080351.
58. Vonk F, Verhagen AP, Twisk JW, Köke AJA, Luiten MWCT, Koes BW. Effectiveness of a behaviour graded activity program versus conventional exercise for chronic neck pain patients. *Eur J Pain*. 2009;13(5):533–41. doi:10.1016/j.ejpain.2008.06.008.

59. Lee H, Hübscher M, Moseley GL, et al. How does pain lead to disability? A systematic review and meta-analysis of mediation studies in people with back and neck pain. *Pain*. 2015;156(6):988–99. doi:10.1097/j.pain.0000000000000146.
60. Balshem H, Helfand M, Sch HJ, et al. GRADE guidelines: 3 . Rating the quality of evidence. 2011;64. doi:10.1016/j.jclinepi.2010.07.015.

Appendix 2.1: Search strategy

Review question:

Which factors predict the development of chronic musculoskeletal neck pain after a first episode of idiopathic, non-traumatic neck pain?

MEDLINE(PubMed)

(chronic OR "non specific" OR nonspecific OR "long standing" OR longstanding OR persistent) AND ("Neck Pain"[Mesh] OR neck pain[tiab] OR neckache*[tiab] OR neck ache*[tiab] OR cervicodynia*[tiab] OR cervicalgia*[tiab] OR cervical pain[tiab] OR cervical ache[tiab] OR cervical aches[tiab]) AND (factor*[tiab] OR affordance*[tiab] OR constraint*[tiab] OR obstacle*[tiab] OR impediment*[tiab] OR enabler*[tiab] OR motivat*[tiab] OR inhibit*[tiab] OR stimulat*[tiab] OR correlat*[tiab] OR determin*[tiab] OR facilitat*[tiab] OR barrie*[tiab])

PsycINFO(OVID)

((chronic OR non specific OR nonspecific OR long standing OR longstanding OR persistent) AND (neck pain OR neckache* OR neck ache* OR cervicodynia* OR cervicalgia* OR cervical pain OR cervical ache*) AND (factor* OR affordance* OR constraint* OR obstacle* OR impediment* OR enabler* OR motivat* OR inhibit* OR stimulat* OR correlat* OR determin* OR facilitat* OR barrie*)).mp.

Embase(Elsevier)

chronic OR 'non specific' OR nonspecific OR 'long standing' OR longstanding OR persistent AND ('neck pain'/exp OR neckache* OR 'neck ache*' OR cervicodynia* OR cervicalgia* OR 'cervical pain' OR 'cervical ache*') AND (factor* OR affordance* OR constraint* OR obstacle* OR impediment* OR enabler* OR motivat* OR inhibit* OR stimulat* OR correlat* OR determin* OR facilitat* OR barrie*) AND [embase]/lim

SPORTDiscus(EBSCO)

(chronic OR "non specific" OR nonspecific OR "long standing" OR longstanding OR persistent) AND (DE "NECK pain" OR "neck pain" OR neckache* OR "neck ache*" OR cervicodynia* OR cervicalgia* OR "cervical pain" OR "cervical ache*") AND (factor* OR affordance* OR constraint* OR obstacle* OR impediment* OR enabler* OR motivat* OR inhibit* OR stimulat* OR correlat* OR determin* OR facilitat* OR barrie*)

CINAHL(EBSCO)

(chronic OR "non specific" OR nonspecific OR "long standing" OR longstanding OR persistent) AND (MH "Neck Pain" OR "neck pain" OR neckache* OR "neck ache*" OR cervicodynia* OR cervicalgia* OR "cervical pain" OR "cervical ache*") AND (factor* OR affordance* OR constraint* OR obstacle* OR impediment* OR enabler* OR motivat* OR inhibit* OR stimulat* OR correlat* OR determin* OR facilitat* OR barrie*)

Grey literature databases

Dart Europe: "neck pain" AND factor*

Open access Theses and Dissertations: "neck pain" AND factor*

NDLTD: "neck pain" AND factor*

Clinical trials.gov: "neck pain" AND factor*

WHO ICTRP: "neck pain" AND factor*

Appendix 2.2: Data extraction table

Authors	Population	N (at baseline)	Patients characteristics	Mean age (SD)	Outcome variables	Follow-up period	N (at follow-up)	Statistical analyses	Recovery	Quality of the study (QUIPS)
Hoving et al. ³⁷	GP NL	183 60.7% F	Pain and/or stiffness of the neck for at least two weeks Previous 6 months no pain	66.7% > 40 yrs	Pain intensity NRS PGIC	7 and 52 weeks	7 weeks 183 (100%) 52 weeks 178 (97%)	Logistic regression analysis Multiple regression	7 weeks 51.4% 52 weeks 63.4% recovered	High risk of bias
Hill et al. ⁴¹	Adults general population UK	1359 61% F (follow-up responders)	1 month period prevalent neck pain	51 yrs (follow-up responders)	Persistent neck pain	12 months	786 (58%)	Logistic regression analysis Multiple regression	381 (48%) neck pain after 1 year	High risk of bias
Vos et al. ³⁹	GP NL	187 64% F	Non-specific neck pain < 6 weeks first episode or after a pain free period > 3 months	Females 38.2, SD 13.3 yrs Males 43.2, SD 14.9 yrs	PGIC	6, 12, 26, and 52 weeks	138 (74%)	Logistic regression analysis Multiple regression	76% recovered or much improved, 47% ongoing pain	High risk of bias
Wirth et al. ³⁸	Chiropractic practices CH	103 60.7% F	First episode acute non-specific neck pain < 4 weeks	38.3 SD 13.8 yrs	PGIC	One week, 1 and 3 months	82 (80%)	Logistic regression analysis Multiple regression	86.6% improved after 3 months	High risk of bias
Schellinghe rhout et al. ⁴⁰	GP NL	468 61% F	Non-specific neck pain Acute and subacute (61%)	45.4 SD 11.8 yrs	PGIC	6 months	Missing value differ per variable (1–43%)	Logistic regression analysis Multiple regression	43% persistent complaints	High risk of bias
Pool et al. ³⁶	GP NL	146	Subacute neck pain	45.1 SD 11.2	GPE NRS pain	12 weeks 52 weeks	12 weeks 146 (100%) 52 weeks 128 (87.7%)	Logistic regression analysis Multiple regression	GPE 12 weeks: 70.5% 52 weeks: 77.2% NRS 12 weeks: 8.6% 52 weeks: 68.2%	High risk of bias

N = number, F = female, N= number of patients, NRS= Numerical rating scale, BQ= Bournemouth questionnaire, PGIC = patient global impression of change, GPE = Global perceived recovery SD = standard deviation, GP = general practice, NL = Netherlands, UK = United Kingdom, CH = Switzerland.

Appendix 2.3: Univariate level of evidence of positive association with a higher pain intensity

Prognostic factors	3 months	12 months	Level of evidence	Overall quality of evidence
Social demographic characteristics				
> age 40		1.04 (0.27–1.80) ³⁷	Moderate evidence for a positive association with a higher pain intensity at 12 months	Low
Hoving et al.				
Age				
Hill et al.				
18–30 years (ref)				
30–44 years		1.5 (0.9–2.6) ⁴¹		
45–59 years		3.4 (2.0–5.7) ⁴¹		
60–75 years		2.1 (1.3–3.4) ⁴¹		
Age (measured in years)	1.0036			
Pool et al.				
Gender (female)	0.38 (0.19–0.76) ³⁶	1.0 (0.8–1.3) ⁴¹	Limited evidence for a positive association with a higher pain intensity at 3 months	Very low
Pool et al.		-0.15 (-91–0.60) ³⁷		
Hoving et al.				
Hill et al.				
Social class				
Hill et al.				
Nonmanual (ref)				
Manual		1.1 (0.8–1.4) ⁴¹		

Appendix 2.3 continues on next page.

Appendix 2.3: Continued

Prognostic factors	3 months	12 months	Level of evidence	Overall quality of evidence
Marital status				
Hill et al.				
Married/partner (ref)				
Other		1.3 (0.9–1.7) ⁴¹		
Children				
Hill et al.				
None (ref)				
1		0.7 (0.4–1.1) ⁴¹		
2		1.2 (0.8–1.9) ⁴¹		
≥ 3		1.1 (0.7–1.6) ⁴¹		
Nonworking				
Hill et al.		1.8 (1.3–2.5)⁴¹	Limited evidence for a positive association with a higher pain intensity at 12 months	Very low
Symptoms				
Low Back Pain				
Hoving et al.		1.7 (1.3–2.3)⁴¹	Moderate evidence for a positive association with a higher pain intensity at 12 months	Very low
Hill et al.		1.13 (0.29–1.97) ³⁷		
Pain intensity at baseline				
Pool et al.	1.10 (0.17–1.19) ³⁶	0.26 (0.07–0.45) ³⁷	Limited evidence for a positive association with a higher pain intensity at 12 months	Very low
Hoving et al.				
Severity of complaints				
Pool et al.	0.78 (0.61–0.91)³⁶		Limited evidence for a positive association with a higher pain intensity at 3 months	Very low

Duration of the neck pain Hoving et al. 2–6 weeks (ref) 7–12 weeks ≥ 13 weeks	Limited evidence for a positive association with a higher pain intensity at 12 months		Very low
		0.07 (-0.76–0.91) ³⁷ 1.03 (0.19–1.86)^{*37}	
Radiating pain below elbow Hoving et al.		0.77 (-0.23–1.71) ³⁷	
Headache (of cervical origin) Pool et al. Hoving et al.	1.67 (0.81–3.33) ³⁶	0.52 (-0.29–1.32) ³⁷	
No change in neck pain previous 2 weeks Hoving et al.		0.66 (-0.08–1.39) ³⁷	
Disturbed sleep due to neck pain Hoving et al.		0.33 (-0.41–1.06) ³⁷	
High severity of physical dysfunctioning Hoving et al.		0.66 (-0.10–1.42) ³⁷	
GCPS (grade) Pool et al. 1 = low intensity 2 = high intensity 3 = Moderately limiting 4 = severely limiting	0.75 (0.25–2.22) ³⁶ 1.04 (0.28–3.85) ³⁶ 1.19 (0.33–4.35) ³⁶		

Appendix 2.3 continues on next page.

Appendix 2.3: Continued

Prognostic factors	3 months	12 months	Level of evidence	Overall quality of evidence
Prior conditions/cause problem				
Previous episodes of neck pain Pool et al. Hoving et al.	1.03 (0.52–2.08) ³⁶	0.83 (0.06–1.59)^{*37}	Limited evidence for a positive association with a higher pain intensity at 12 months	Very low
Neck injury/Traumatic cause Hoving et al. Hill et al.		1.5 (1.1–2.2) ^{*41} 0.72 (-0.71–1.25) ³⁷	Conflicting evidence for a positive association with a higher pain intensity at 12 months	Very low
Physical activities				
Standing/walking in last job ≥ 2 hours Hill et al.		1.2 (0.9–1.7) ⁴¹		
Driving in last job ≥ 4 hrs Hill et al.		0.8 (0.5–1.2) ⁴¹		
Digging/shoveling in last job Hill et al.		0.8 (0.4–1.7) ⁴¹		
Sitting in last job ≥ 2 hours Hill et al.		0.9 (0.6–1.2) ⁴¹		
Lifting in last job ≥ 25 lb weights Hill et al.		1.3 (1.0–1.8) ^{*41}	Limited evidence for a positive association with a higher pain intensity at 12 months	Very low
Gardening at last once or twice a week Hill et al.		0.8 (0.6–1.0) ^{*41}	Limited evidence for a negative association with a higher pain intensity at 12 months	Very low

Do-it-yourself work often Hill et al.	1.0 (0.7–1.4) ⁴¹		
Walking each day > 30 min Hill et al.	1.1 (0.8–1.4) ⁴¹		
Cycling each day Hill et al.	2.0 (1.3–3.2)⁴¹	Limited evidence for a positive association with a higher pain intensity at 12 months	Very low
TV hours > 3 hrs per day Hill et al.	0.9 (0.7–1.3) ⁴¹		
Physical activity Less than average Hill et al.	1.4 (1.0–1.9) ⁴¹	Limited evidence for a positive association with a higher pain intensity at 12 months	Very low
Psychological factors			
Catastrophizing (PCCL) Pool et al.	2.38 (0.98–5.88) ³⁶		
Coping (PCCL) Pool et al.	1.12 (0.77–1.67) ³⁶		
Internal pain control (PCCL) Pool et al.	0.82 (0.68–1.41) ³⁶		
External pain control (PCCL) Pool et al.	1.03 (0.72–1.47) ³⁶		
TSK (higher score) Pool et al.	1.06 (1.00–1.12)³⁶	Limited evidence for a positive association with a higher pain intensity at 3 months	Very low

Appendix 2.3 continues on next page.

Appendix 2.3: Continued

Prognostic factors	3 months	12 months	Level of evidence	Overall quality of evidence
Somatization (4DSQ) Pool et al.	1.09 (1.01–1.18) ³⁶		Limited evidence for a positive association with a higher pain intensity at 3 months	Very low
Fear (4DSQ) Pool et al.	1.75 (1.11–2.78) ³⁶		Limited evidence for a positive association with a higher pain intensity at 3 months	Very low
Distress (4DSQ) Pool et al.	1.39 (0.95–2.00) ³⁶			
Depression (4DSQ) Pool et al.	1.52 (0.81–2.86) ³⁶			
Job satisfaction Hill et al.		1.1 (0.7–1.7) ⁴¹		
Satisfaction at not working Hill et al.		1.4 (0.9–2.2) ⁴¹		
General health				
BMI				
Hill et al.				
< 22.5 (ref)				
22.5–25.0		1.1 (0.8–1.7) ⁴¹		
25.1–27.4		1.0 (0.7–1.6) ⁴¹		
≥ 27.5		1.4 (0.9–2.1) ⁴¹		
Smoking status				
Hill et al.				
Never (ref)				
Past		1.1 (0.7–1.5) ⁴¹		
Current		1.0 (0.7–1.6) ⁴¹		

Alcohol intake Hill et al. < 3 days per week ≥ 3 days per week		Limited evidence for a negative association with a higher pain intensity at 12 months	Very low
Perceived General health Hill et al. Excellent (ref) Good Fair Poor		Limited evidence for a positive association with a higher pain intensity at 12 months	Very low
GHQ Hill et al. < 8 (ref) 8–11 12–17 ≥ 18 poor psychological health		Limited evidence for a positive association with a higher pain intensity at 12 months	Very low
Remaining factors			
Patients preference Pool et al. None Pt Mt	0.43 (0.15–1.23) ³⁶ 0.86 (0.39–1.25) ³⁶		
GP attitude Pool et al. Purely biomedical (ref) More biomedical	0.67 (0.24–1.85) ³⁶ 0.46 (0.17–1.12) ³⁶		

OR^{41,36}. Regression coefficient, 95% CI > 0 bad / < 0 good for pain intensity³⁷. * = Significant prognostic value. Variables that remained after the multivariate analysis shown in bold. GCPS = Graded Chronic Pain Scale. GHQ = General health questionnaire. GP = General Practitioner. PCCL = Pain Coping and Cognition list. TSK = Tampa Scale of Kinesiophobia. 4DSQ = Four Dimension Symptomatology Questionnaire.

Appendix 2.4: Univariate level of evidence of positive association with perceived non-recovery

Prognostic factors	3 months	6 months	12 months	Level of evidence	Overall quality of evidence
Social demographic characteristics					
Age ≥ 40 years Pool et al. Hoving et al.	1.03 (0.98–1.09) ³⁶		2.94 (1.45–5.88)³⁷	Limited evidence for perceived non-recovery at 12 months	Low
Age (in years) Pool et al. Schellingerhout et al.	1.01 (0.98–1.04) ³⁶	0.88 (0.79–0.99) ⁴⁰		Limited evidence for a better outcome at 6 months	Very low
Age-square Schellingerhout et al.		1.00 (1.00–1.06) ⁴⁰		Limited evidence for perceived non-recovery at 6 months	Very low
Gender (female) Pool et al. Hoving et al. Vos et al. Schellingerhout et al.	2.00 (1.10–4.35) ³⁶	0.98 (0.65–1.46) ⁴⁰	2.5 (0.99–6.25)³⁹ 0.69 (0.37–1.28) ³⁷	Limited evidence for a better outcome at 3 months	Very low
Level of education					
Schellingerhout et al.					
High (ref)		1.26 (0.79–2.02) ⁴⁰			
Middle		1.23 (0.75–2.02) ⁴⁰			
Low					
Employment status (yes = 1) Schellingerhout et al.		0.60 (0.39–0.92) ⁴⁰		Limited evidence for a better outcome at 6 months	Very low

Symptoms			
Low Back Pain Hoving et al. Schellingerhout et al.	2.07 (1.31–3.27) ^{*40}	2.17 (1.06–4.35)^{*37}	Limited evidence for perceived non-recovery at 6 and 12 months Low for 6 months Very low for 12 months
Severe initial pain Pool et al. Vos et al. Schellingerhout et al.	1.14 (0.76–1.67) ³⁶ 0.70 (0.46–1.07) ⁴⁰	1.04 (0.52–2.09) ³⁹	
Severe initial pain square Schellingerhout et al.	1.05 (1.01–1.09)^{*40}		Limited evidence for perceived non-recovery at 6 months Very low
Severity of complaints Pool et al.	0.95 (0.75–1.22) ³⁶		
Duration of complaints > 2 weeks Vos et al.		2.44 (1.03–5.56)^{*39}	Limited evidence for perceived non-recovery at 12 months Very low
Duration current episode Hoving et al. Schellingerhout et al. 1–3 months > 3 months	0.68 (0.38–1.22) ⁴⁰ 1.25 (0.68–2.31) ⁴⁰	1.14 (0.53–2.44) ³⁷ 2.04 (0.97–4.35) ³⁷	
Pain in the upper part of the neck Vos et al.		1.64 (1.22–2.17)^{*39}	Limited evidence for perceived non-recovery at 12 months Very low

Appendix 2.4 continues on next page.

Appendix 2.4: Continued

Prognostic factors	3 months	6 months	12 months	Level of evidence	Overall quality of evidence
Accompanying headache Pool et al. Hoving et al. Vos et al. Schellingerhout et al.	3.45 (1.41–8.33)^{*3,6}	1.92 (1.23–3.00) ^{*40}	3.33 (1.35–8.33) ^{*39} 1.37 (0.69–2.70) ³⁷	Limited evidence for perceived non-recovery at 3 and 6 months. Moderate evidence for perceived non-recovery at 12 months.	Low for 3, 6 and 12 months
Radiating pain below elbow Hoving et al.	1.49 (0.66–3.33) ³⁷				
Radiating to the back Vos et al.			1.45 (1.09–1.92)^{*39}	Limited evidence for perceived non-recovery at 12 months	Very low
Radiating pain (yes = 1) Schellingerhout et al.		0.66 (0.45–0.97)^{*40}		Limited evidence for a better outcome at 6 months	Very low
No change in neck pain previous 2 weeks Hoving et al.			2.63 (1.39–4.76)^{*37}	Limited evidence for perceived non-recovery at 12 months	Very low
Disturbed sleep due to neck pain Hoving et al.	0.88 (0.48–1.61) ³⁷				
Accompanying dizziness (yes = 1) Schellingerhout et al.	1.47 (0.99–2.17) ⁴⁰				
High severity of physical dysfunctioning Hoving et al.	1.59 (0.84–3.03) ³⁷				

GCPS (grade) Pool et al. 1 = low intensity 2 = high intensity 3 = moderately limiting 4 = severely limiting							
		0.56 (0.18–1.75) ³⁶ 1.64 (0.44–6.25) ³⁶ 0.77 (0.20–3.03) ³⁶		1.05 (1.02–1.08) ^{*40}	1.08 (1.01–1.14) ^{*39}	Limited evidence for perceived non-recovery at 6 and 12 months	Very low
Total score on the NDI (higher score) Vos et al. Schellingerhout et al.							
Total score on the ALBPSQ Vos et al.					1.02 (1.00–1.03) ^{*39}	Limited evidence for perceived non-recovery at 12 months	Very low
Prior conditions/cause problem							
Previous episodes of neck pain Pool et al. Hoving et al. Vos et al. Schellingerhout et al.				1.56 (0.75–3.23) ³⁶	1.20 (1.03–1.41) ^{*39} 1.75 (0.90–3.45) ³⁷	Limited evidence for perceived non-recovery at 6 months. Moderate evidence for perceived non-recovery at 12 months.	Low for 6 months Very low for 12 months
Psychological factors							
Catastrophizing (PCCL) Pool et al.				1.75 (0.68–4.55) ³⁶			
Coping (PCCL) Pool et al.				0.82 (0.54–1.23) ³⁶			
Internal pain control (PCCL) Pool et al.				0.83 (0.56–1.25) ³⁶			

Appendix 2.4 continues on next page.

Appendix 2.4: Continued

Prognostic factors	3 months	6 months	12 months	Level of evidence	Overall quality of evidence
External pain control(PCCL) Pool et al.	0.93 (0.62–1.37) ³⁶				
TSK (higher score) Pool et al. Schellingerhout et al.	1.05 (1.00–1.11) ^{*36}	1.03 (1.01–1.06) ^{*40}		Limited evidence for perceived non- recovery at 3 and 6 months	Very low for 3 months Low for 6 months
Somatization (4DSQ) Pool et al.	1.04 (0.95–1.11) ³⁶				
Fear (4DSQ) Pool et al.	1.27 (0.81–1.96) ³⁶				
Distress (4DSQ) Pool et al.	1.08 (0.72–1.61) ³⁶				
4DSQ Depression Pool et al.	1.33 (0.71–2.5) ³⁶			Limited evidence for perceived non- recovery at 3 months	Very low
General health					
EuroQOL VAS Schellingerhout et al.		0.99 (0.98–1.00) ^{*40}		Limited evidence for a better outcome at 6 months	Very low
Remaining factors					
Patients preference Pool et al. Schellingerhout et al.					
None					
Pt	0.25 (0.05–1.15) ³⁶	0.77 (0.45–1.32) ⁴⁰			
Mt	0.58 (0.69–1.45) ³⁶	1.19 (0.73–1.93) ⁴⁰			

GP attitude Pool et al. Purely biomedical (ref) More biomedical Neutral	2.13 (0.76–5.88) ³⁶ 0.46 (0.16–1.35) ³⁶			
Treated for neck pain in the past (yes = 1) Schellingerhout et al.	1.77 (1.20–2.61) ^{*40}		Limited evidence for perceived non- recovery at 6 months	Very low
Treated by physiotherapist before Vos et al		1.25 (1.10–1.89) ^{*39}	Limited evidence for perceived non- recovery at 12 months	Very low
Treated by manual therapist before Vos et al		1.28 (1.00–1.67) ^{*39}	Limited evidence for perceived non- recovery at 12 months	Very low
GP advised to wait and see Vos et al		0.26 (0.07–0.93)^{*39}	Limited evidence for a better outcome at 12 months	Very low
GP advised to improve posture Vos et al		0.96 (0.72–1.28) ³⁹		
GP prescribed medication Vos et al		1.64 (0.81–3.33) ³⁹		
GP instructed in physical exercises Vos et al		0.93 (0.66–1.32) ³⁹		

Results shown in OR = Odds Ratio > 1 positive association, < 1 negative association with non-recovery. * = Significant prognostic value. Variables that remained after the multivariate analysis shown in bold. ALBPSQ = Acute Low Back Pain Screening Questionnaire EuroQOL = Quality of Life Scale. GCP5 = Graded Chronic Pain Scale. GP = General Practitioner. NDI = Neck Disability Index. PCCL = Pain Coping and Cognition list. TSK = Tampa Scale of Kinesiophobia. 4DSQ = Four Dimension Psychological Symptomatology Questionnaire.

Strong	Moderate	Limited	Conflicting	No evidence

Appendix 2.5: Grading assessment quality of evidence for a higher pain intensity

Prognostic factor for pain intensity	# Participants	# Studies	Phase	Study limitations	Inconsistency	Indirectness	Imprecision	Publication bias	Moderate/large effect size	Dose effect	Overall quality
Age	1,542	2	1	X	✓	✓	✓	X	✓	X	++
Gender (female)	146	1	1	X	X	✓	X	X	X	X	+
Non-working	1,359	1	1	X	X	✓	X	X	X	X	+
Low Back Pain	1,542	2	1	X	✓	✓	✓	X	X	X	+
Pain intensity	183	1	1	X	X	✓	X	X	✓	X	+
Severity of complaints	146	1	1	X	X	✓	X	X	X	X	+
Duration neck pain	183	1	1	X	X	✓	X	X	X	X	+
Previous episodes neck pain	183	1	1	X	X	✓	X	X	X	X	+
Neck injury	1,542	2	1	X	✓	✓	✓	X	X	X	+
Lifting in last job	1,359	1	1	X	X	✓	X	X	X	X	+
Gardening	1,359	1	1	X	X	✓	X	X	X	X	+
Cycling	1,359	1	1	X	X	✓	X	X	X	X	+
Physical activity	1,359	1	1	X	X	✓	X	X	X	X	+
TSK (higher score)	146	1	1	X	X	✓	X	X	X	X	+
Somatisation	146	1	1	X	X	✓	X	X	X	X	+
Fear	146	1	1	X	X	✓	X	X	X	X	+
Alcohol intake	1,359	1	1	X	X	✓	X	X	X	X	+
Perceived General Health	1,359	1	1	X	X	✓	X	X	X	X	+
GHQ (higher score, poor psychological health)	1,359	1	1	X	X	✓	X	X	X	X	+

Phase, phase of investigation. For GRADE factors: ✓, no serious limitations; X, serious limitations (or not applicable; for publication bias, imprecision and inconsistency only one study available). For overall quality of evidence: +, very low; ++, low. TSK = Tampa Scale of Kinesiophobia, GHQ = General Health Questionnaire.

Appendix 2.6: Grading assessment quality of evidence for the outcome variable perceived non-recovery

Prognostic factor for perceived non-recovery	# Participants	# Studies	Phase	Study limitations	Inconsistency	Indirectness	Imprecision	Publication bias	Moderate/large effect size	Dose effect	Overall quality
Age ≥ 40 years	183	1	1	X	X	✓	X	X	✓	X	+
Age (in years)	468	1	3	X	X	✓	X	X	X	X	+
Age-square	468	1	3	X	X	✓	X	X	X	X	+
Gender	146	1	1	X	X	✓	X	X	X	X	+
Employment status (yes = 1)	468	1	3	X	X	✓	X	X	X	X	+
Low back pain											
6 months	468	1	3	X	✓	✓	✓	X	X	X	++
12 months	183	1	1	X	✓	✓	✓	X	X	X	+
Severe initial pain square	468	1	3	X	X	✓	X	X	X	X	+
Duration of complaints > 2 weeks	187	1	1	X	X	✓	X	X	X	X	+
Pain in the upper part of the neck	187	1	1	X	X	✓	X	X	X	X	+
Accompanying headache											
3 months	146	1	1	X	✓	✓	✓	X	✓	X	++
6 months	468	1	3	X	✓	✓	✓	X	X	X	++
12 months	370	2	1	X	✓	✓	✓	X	✓	X	++
Radiating to the back	187	1	1	X	X	✓	X	X	X	X	+
Radiating pain (yes = 1)	468	1	3	X	X	✓	X	X	X	X	+
No change in neck pain previous 2 weeks	183	1	1	X	X	✓	X	X	✓	X	+

Appendix 2.6 continues on next page.

Appendix 2.6: Continued

Prognostic factor for perceived non- recovery	# Participants	# Studies	Phase	Study limitations	Inconsistency	Indirectness	Imprecision	Publication bias	Moderate/ large effect size	Dose effect	Overall quality
Total score on the NDI (higher score)											
6 months	468	1	3	X	X	✓	X	X	X	X	+
12 months	187	1	1	X	X	✓	X	X	X	X	+
Total score on the ALBPSQ	187	1	1	X	X	✓	X	X	X	X	+
Previous episodes of neck pain											
6 months	468	1	3	X	✓	✓	✓	X	X	X	++
12 months	370	2	1	X	✓	✓	✓	X	X	X	+
Traumatic cause	468	1	3	X	X	✓	X	X	X	X	+
TSK (higher score)											
3 months	146	1	1	X	✓	✓	✓	X	X	X	+
6 months	468	1	3	X	✓	✓	✓	X	X	X	++
Depression (4DSQ)	146	1	1	X	X	✓	X	X	X	X	+
EuroQOL VAS	468	1	3	X	X	✓	X	X	X	X	+
Treated for neck pain in past	468	1	3	X	X	✓	X	X	X	X	+
Treated by FT before	187	1	1	X	X	✓	X	X	X	X	+
Treated by MT before	187	1	1	X	X	✓	X	X	X	X	+
GP wait and see advise	187	1	1	X	X	✓	X	X	✓	X	+

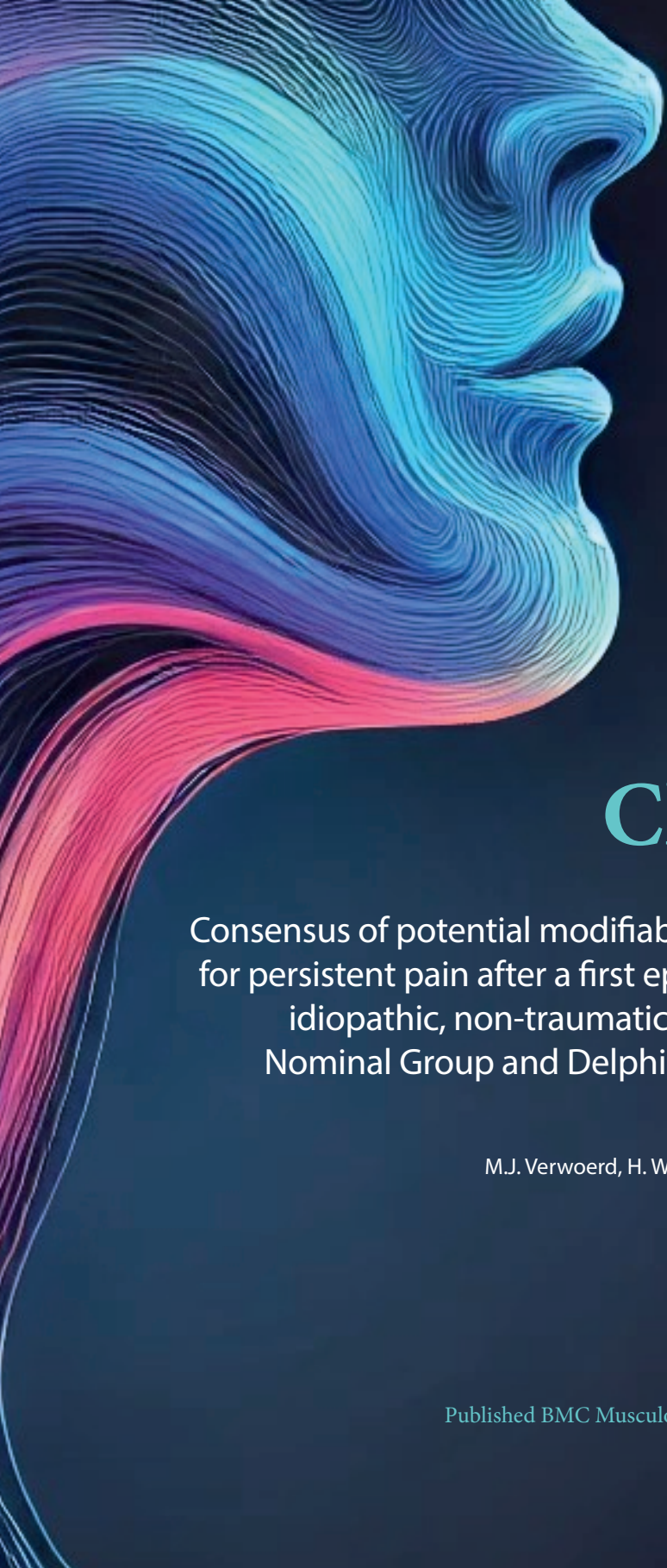
Phase, phase of investigation. For GRADE factors: ✓, no serious limitations; X, serious limitations (or not applicable; for publication bias, imprecision and inconsistency only one study available). For overall quality of evidence: +, very low; ++, low. NDI = Neck Disability Index, ALBPSQ = Acute Low Back Pain Questionnaire, TSK = Tampa Scale of Kinesiophobia, 4DSQ = Four Dimension Psychological Symptomatology Questionnaire, EuroQOL = Quality of Life Scale, GP = General Practitioner.

Appendix 2.7: Reviewer agreement for full text screening after screening title and abstract

1. Kjellman G, Öberg B, Hensing G, Alexanderson K. A 12-year follow-up of subjects initially sicklisted with neck/shoulder or low back diagnoses. *Physiother Res Int*. 2001;6(1):52-63
2. Ailliet L, Rubinstein SM, Hoekstra T, van Tulder MW, de Vet HC. Adding Psychosocial Factors Does Not Improve Predictive Models for People With Spinal Pain Enough to Warrant Extensive Screening for Them at Baseline. *Phys Ther*. 2016;96(8):1179-1189
3. Côté P, Cassidy JD, Carroll LJ, Kristman V. The annual incidence and course of neck pain in the general population: A population-based cohort study. *Pain*. 2004;112(3):267-273
4. Pool JJ, Ostelo RW, Knol D, Bouter LM, de Vet HC. Are psychological factors prognostic indicators of outcome in patients with sub-acute neck pain? *Man Ther*. 2010;15(1):111-116
5. Vos CJ, Verhagen AP, Passchier J, Koes BW. Clinical course and prognostic factors in acute neck pain: An inception cohort study in general practice. *Pain Med (USA)*. 2008;9(5):572-580
6. Badcock LJ, Lewis M, Hay EM, Croft PR. Consultation and the Outcome of Shoulder-Neck Pain: A Cohort Study in the Population. *J Rheumatol*. 2003;30(12):2694-2699
7. Johansen JB, Røe C, Bakke ES, Mengshoel AM, Storheim K, Andelic N. The determinants of function and disability in neck patients referred to a specialized outpatient clinic. *Clin J Pain*. 2013;29(12):1029-1035
8. Paksaihol A, Janwantanakul P, Lawsirirat C. Development of a Neck Pain Risk Score for Predicting Non-specific Neck Pain with Disability in Office Workers: a 1-Year Prospective Cohort Study. *J Manipulative Physiol Ther*. 2014 09;37(7):468-475
9. Boersma K, Linton SJ. Expectancy, fear and pain in the prediction of chronic pain and disability: A prospective analysis. *Eur J Pain*. 2006;10(6):551-557
10. Hurwitz EL, Goldstein MS, Morgenstern H, Chiang L. The impact of psychosocial factors on neck pain and disability outcomes among primary care patients: results from the UCLA Neck Pain Study. *Disabil Rehabil*. 2006;28(21):1319-1329
11. Wirth B, Humphreys BK, Peterson C. Importance of psychological factors for the recovery from a first episode of acute non-specific neck pain - a longitudinal observational study. *Chiropr Man Therap*. 2016;24:1-10
12. Mercado AC, Carroll LJ, Cassidy JD, Cote P. Passive coping is a risk factor for disabling neck or low back pain. *Pain*. 2005;117(1-2):51-57
13. Kovacs FM, Seco J, Royuela A, Melis S, Sánchez C, Díaz-Arribas MJ, et al. Patients with neck pain are less likely to improve if they experience poor sleep quality: a prospective study in routine practice. *Clin J Pain*. 2015 08;31(8):713-721
14. Leaver AM, Maher CG, McAuley JH, Jull G, Latimer J, Refshauge KM. People seeking treatment for a new episode of neck pain typically have rapid improvement in symptoms: an observational study. *J Physiother*. 2013;59(1):31-37
15. Hill J, Lewis M, Papageorgiou AC, Dziedzic K, Croft P. Predicting persistent neck pain: a 1-year follow-up of a population cohort. *Spine*. 2004 08;29(15):1648-1654
16. Dagfinrud H, Storheim K, Magnussen LH, Ødegaard T, Hoftaniska I, Larsen LG, 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. *Manual Ther*. 2013;18(2):124-129
17. Grooten WJA. Predictors for persistent neck/shoulder pain, medical care-seeking due to neck/shoulder pain and sickness absence. *Clin Rehabil*. 2007;21(7):648-659
18. Webb R, Brammah T, Lunt M, Urwin M, Allison T, Symmons D. Prevalence and predictors of intense, chronic, and disabling neck and back pain in the UK general population. *Spine*. 2003;28(11):1195-1202
19. Hoving JL, De Vet HCW, Twisk JWR, DevillÃ WLJM, Van DW, Koes BW, et al. Prognostic factors for neck pain in general practice. *Pain*. 2004;110(3):639-645
20. Kjellman G, Skargren E, Åberg B. Prognostic factors for perceived pain and function at one-year follow-up in primary care patients with neck pain. *Disabil Rehabil*. 2002;24(7):364-370
21. Hellsing AL, Linton SJ, Kalvemark M. A prospective study of patients with acute back and neck pain in Sweden. *Phys Ther*. 1994;74(2):116-128
22. Keijsers E, Feleus A, Miedema HS, Koes BW, Bierma-Zeinstra SM. Psychosocial factors predicted nonrecovery in both specific and nonspecific diagnoses at arm, neck, and shoulder. *J Clin Epidemiol*. 2010;63(12):1370-1379

23. Shahidi B, CurranEverett D, Maluf KS. Psychosocial, physical, and neurophysiological risk factors for chronic neck pain: A prospective inception cohort study. *J Pain*. 2015;16(12):1288-1299
24. Croft PR, Lewis M, Papageorgiou AC, Thomas E, Jayson MIV, Macfarlane GJ, et al. Risk factors for neck pain: A longitudinal study in the general population. *Pain*. 2001;93(3):317-325
25. Christensen JO, Knardahl S. Time-course of occupational psychological and social factors as predictors of new-onset and persistent neck pain: A three-wave prospective study over 4years. *Pain*. 2014;155(7):1262-1271





Chapter 3

Consensus of potential modifiable prognostic factors
for persistent pain after a first episode of nonspecific
idiopathic, non-traumatic neck pain: Results of
Nominal Group and Delphi Technique approach

M.J. Verwoerd, H. Wittink, F. Maissan, R.J.E.M. Smeets

Published BMC Musculoskeletal Disorders, 2020, October

Background: Identify and establish consensus regarding potential prognostic factors for the development of chronic pain after a first episode of idiopathic, non-traumatic neck pain.

Design: This study used two consensus group methods: a modified Nominal Group (m-NGT) and a Delphi Technique.

Methods: The goal of the m-NGT was to obtain and categorize a list of potential modifiable prognostic factors. These factors were presented to a multidisciplinary panel in a two-round Delphi survey, which was conducted between November 2018 and January 2020. The participants were asked whether factors identified are of prognostic value, whether these factors are modifiable, and how to measure these factors in clinical practice. Consensus was a priori defined as 70% agreement among participants.

Results: Eighty-four factors were identified and grouped into seven categories during the expert meeting using the modified NGT. A workgroup reduced the list to 47 factors and grouped them into 12 categories. Of these factors, 25 were found to be potentially prognostic for chronification of neck pain (> 70% agreement). Nineteen out of these 25 factors were found to be potentially modifiable by physiotherapists based on a two-round Delphi survey.

Conclusion: Based on an expert meeting (m-NGT) and a two-round Delphi survey, our study documents consensus (> 70%) on 25 prognostic factors. Nineteen out of these 25 factors were found to be modifiable, and most factors were psychological in nature.

Key words: Prognostic factors, chronic neck pain, idiopathic neck pain, prognostic factors, Delphi survey

Background

Commonly it is assumed that most episodes of acute idiopathic neck pain will resolve with or without treatment. However, Childs et al. argue that rates of persistent neck pain are substantial.¹ It is suggested that the prognosis of acute neck pain is worse than currently recognized.² Twenty-four to 37% of individuals who experience neck pain will report persistent problems for at least 12 months.³ In the Netherlands, neck pain is the most prevalent disorder presented at physiotherapy practices.⁴

The reported effect of physiotherapy treatment of chronic musculoskeletal pain is, at best, only moderate.^{5–7} Prevention of chronicity must occur in the (sub)acute phase of musculoskeletal pain. Knowledge of prognostic, potentially modifiable factors can help health care providers to improve clinical decision-making and is a likely key in combatting chronification of idiopathic neck pain.

A recent systematic review showed limited evidence to support prognostic factors that are associated with pain or perceived non-recovery up until one year after the onset of neck pain.⁸ The quality of the available evidence was graded as low to very low and included only a few modifiable factors. Psychosocial factors as passive coping, catastrophizing, fear-avoidance beliefs, depressive symptoms, distress, and anxiety are potentially modifiable factors that were found to be associated with chronic neck pain, whiplash related neck pain, and low back pain.^{9,10,19,11–18} These findings concern other subgroups of musculoskeletal pain, and can therefore not be generalized to patients with idiopathic nonspecific, non-traumatic, acute or subacute neck pain.

It is known that neurophysiological changes in chronification of pain are modulated by psychosocial factors.²⁰ It is therefore surprising that prior research on chronification of idiopathic nonspecific, non-traumatic, acute or subacute musculoskeletal neck pain is frequently done from a biomedical perspective only. At this stage, it is still unclear which factors are potentially prognostic and modifiable by physiotherapists in this subgroup.

Starting this study with a wider view (i.e. biopsychosocial framework), seems to be important.

Purpose of the study

To establish consensus regarding potential prognostic factors for the development of chronic pain after a first episode of idiopathic, non-traumatic neck pain and whether experts consider these factors as modifiable by physiotherapy interventions, by using a modified Nominal Group Technique (m-NGT) and a Delphi survey instrument.

Method

Study design

This study used two consensus group methods; a m-NGT and Delphi Technique.^{21,22} The study was conducted between November 2018 and January 2020. Ethical approval and consent to participate in our Delphi and expert meeting was not required based on the Dutch Medical Research Involving Human Subjects Act (WMO). Figure 3.1 presents the flow-chart of our study.

Expert meeting

We conducted a m-NGT meeting. In general, NGT uses a highly structured meeting to gather information from relevant experts about a pre-specified topic with a focus on a single goal.²¹ This technique comprises four stages: silent generation, round robin, clarification and ranking.²³ The goal in this study was to identify prognostic factors for persistent pain after a first episode of idiopathic, non-specific neck pain to include in a Delphi for consensus. Therefore, we did not complete the ranking stage as is described in a classic NGT but categorized the prognostic factors.

Selection of participants

A NGT usually involving 5–12 experts in the field.²² Our m-NGT group consisted of 11 experts plus two members of the research team. The two members of the research team facilitated the process and were specifically instructed not to influence the participants.²² Being an expert entails the acquisition of experience or knowledge of a particular topic.²⁴ The experts were either working in (1) specialized physiotherapy clinics for nonspecific neck pain patients, and/or (2) working in neck pain research, and/or (3) were academic teachers with a special focus on the neck. To reach a heterogeneous group, we have taken into account a reliable distribution in credentials, occupation at the time of the study, and specialization. The participants of the expert group meeting were selected from the ‘Pain Community’ of

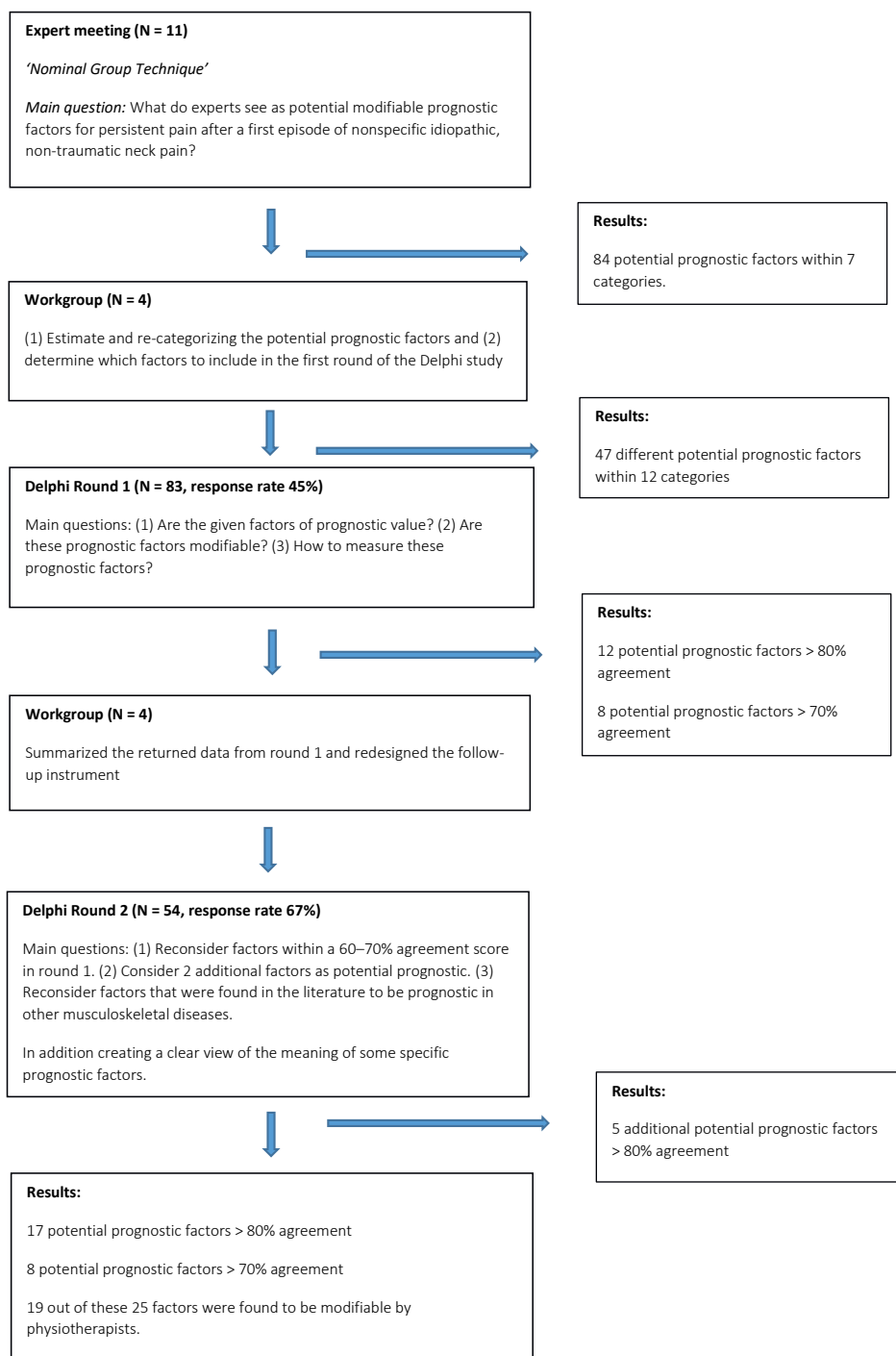


Figure 3.1: Flow-chart study.

the University of Applied Sciences in Utrecht and supplemented by experts from the national network of our research group.

Procedure

Before the expert meeting took place, each participant received a digital file consisting of (i) a summary of the results of a recently performed systematic review on prognostic factors for persistent neck pain,⁸ and (ii) an introduction to our consensus study. Knowledge of these results was the starting point of our expert meeting. The expert meeting followed 4 steps:

- (1) Introduction of the structure of the meeting and the main question of the meeting: ‘What do experts see as potential modifiable prognostic factors for persistent pain after a first episode of nonspecific idiopathic, non-traumatic neck pain?’;
- (2) Brainstorming and writing down ideas about potential modifiable prognostic factors by each participant (10 minutes);
- (3) Presenting, operationalizing and generating more ideas in groups of 2 to 3 participants (this stage takes as much time as needed until no new ideas are forthcoming²⁵);
- (4) Presenting the operationalized ideas to all experts, followed by a group discussion (30 minutes). Towards the end of the discussion the prognostic factors were categorized.

Data analysis

The data was analyzed by a workgroup of four research and clinical experts (HW, MV, FM, ER). The analysis included (1) assessing for overlapping factors (2) re-categorizing the biomedical prognostic factors, and (3) re-categorizing the psychological factors. For re-categorizing psychological factors, an expert in physiotherapy in mental health and psychology was also consulted.

Delphi survey

Selection of participants

Participants were selected via purposive sampling to ensure that each participant had in-depth knowledge of the problem.

Our sampling started at a Dutch/Belgium multidisciplinary research consortium ‘pain in motion’ that focuses on improving the understanding of biopsychosocial mechanisms of pain. Then a search in the PubMed database was performed for the identification of participants across the world with diverse backgrounds to guarantee an international base of knowledge. Experts were eligible to participate if (1) they were clinicians with a large experience in the specific area, and/or (2) they (co)authored at least two peer-reviewed publications in the field of nonspecific neck pain and physiotherapy.

An invitation to participate was sent to 185 eligible candidates.

Procedure

We conducted a two-round Delphi survey. The factors included in the Delphi survey were taken from our systematic review and the expert meeting, as described earlier.[8] Generating data by other qualitative studies for the first round of a Delphi questionnaire is a common and widely accepted method.^{26–28}

We sent a digital questionnaire to survey participants in April 2019. The survey contained a letter introducing the study, an invitation to participate, and instructions for completing the questionnaire. If the questionnaire was not returned within 3 weeks of postage, a reminder email was sent after 3 and 5 weeks. Only questionnaires received up to 6 weeks after the first mailing were included in the analysis.

In the first round of the Delphi survey, participants were asked to answer questions in three subsections (see Appendix 3.1). First, indicate whether the given factors are of prognostic value; second, indicate whether these factors are modifiable or not; and third indicate how to measure these factors. Each subsection also allowed for open commenting. In addition, we asked the participants explicitly to comment on the way of categorizing the psychological factors. Only participants who considered a factor of prognostic value had to answer the questions in subsections two and three.

Although there is no official guideline on optimal consensus, the minimum level of agreement was set at 70%, as suggested in current literature.^{29–32}

The workgroup (MV, HW, FM, RS) summarized the survey data of round 1 and designed a follow-up questionnaire to be surveyed in the second round (see Appendix 3.2). The factors on which consensus was reached were not questioned in the second round.

We included the following factors in our second round questionnaire; (i) a prognostic modifiable factor with a 60–70% agreement score (to avoid false-negative findings), (ii) prognostic factors added by participants in the first round, and (iii) factors that did not reach a sufficient agreement score in the first round, though they were found of prognostic value for other musculoskeletal diseases in the literature. All other factors with a below 60% agreement score were excluded.

In case there was ambiguity about the meaning of specific factors added by participants, the participants were asked to clarify these factors in the second-round questionnaire.

The participants of our Delphi survey were mainly experts in musculoskeletal (neck) pain, but not in measurement tools. Therefore, we only used the first Delphi round to get an indication of how to measure these potentially prognostic factors in research and practice, and not to reach consensus.

Results

Expert meeting

Table 3.1 describes the characteristics of the participants of our expert meeting. Our 11 professionals indicated 84 factors to be prognostic for chronification of neck pain. They categorized them into 7 categories; communication, social support, work-related, pain-related, lifestyle, biomedical/ biomechanical, and psychological (including thoughts, feelings and behavior).

Workgroup

Our workgroup (MV, HW, FM, ER) and our consulted expert analyzed and grouped the 84 potential prognostic factors into 47 factors within 12 categories; social demographic, work-related, symptoms, prior conditions, general factors, cognition, emotions, behavior, perceptions, motivation, vulnerability and remaining (health care provider attitude and therapeutic relation) factors. We did so because (i) there was a strong overlap between a number of these 84 factors, and (ii) the 7 categories were too broad and therefore not specific enough. Table 3.2 presents all factors and categories.

Table 3.1: Demographics of participants at the expert meeting (n = 11)

Gender	Male = 8 Female = 3
Credentials	PhD = 1 PhD student = 2 MSc = 6 BSc = 2
Occupation at the time of the study*	Academic researcher = 3 Academic teacher = 5 Active practicing musculoskeletal PT = 8
Specialization	Orthopedic Manual PT = 2 PT in Mental Health = 6 Medical doctor = 1 Psychologist = 1 Regular PT = 1

* A number of participants have a dual function. Abbreviations: PhD, Doctor of Philosophy; MSc, Master of Science; BSc, Bachelor of Science; PT, Physiotherapist.

Delphi survey

First round

The first-round questionnaire was returned by 83 participants (response rate 45%). The most common professional backgrounds of the participants were researchers with a specialization in neck or chronic pain and orthopedic manual therapists. Table 3.3 describes the characteristics of the participants in round 1 and 2 of our Delphi survey.

Eight of the 47 potential prognostic factors achieved over 70% agreement, and twelve factors achieved over 80% agreement. Two potentially prognostic factors were also added by participants: orofacial pain and the potential to self-modify posture during work. There was only one participant who comment on the way we categorized our psychological factors. Based on this comment, we did not changed our categories.

Table 3.2 and 3.4 describe the consensus agreement of prognostic value and modifiability on prognostic factors.

Second round

The second-round questionnaire was sent to all participants of the first round who submitted answers. The second-round questionnaire was returned by 54 participants (response rate 67%). Lack of participation was not associated with a geographic area or professional background.

Table 3.2: Consensus agreement of prognostic factors Delphi survey

Prognostic factors	Number of participants per factor Round 1	Percentage agreement (yes) Round 1	Number of participants per factor Round 2	Percentage Agreement (yes) Round 2
Social demographic				
Gender	80	56.25%	-	-
Age	80	65%	-	--
Social class	80	56.25%	-	-
Education level	80	66.25%	-	--
Marital status	80	11.24%	-	-
Work-related factors				
Employment status	80	53.75%	-	-
Happiness in work**	80	86.25%	-	-
Physical work	80	53.75%	-	-
Symptoms				
Pain intensity at baseline**	80	65%	-	87.50%
Duration of the neck pain*	80	72.50%	-	-
<i>Disturbed sleep due to neck pain</i>	80	60%	-	-
Reported pain in different body regions*	80	78.75%	-	-
High severity of disability	80	51.25%	-	-
High severity of experienced disability**	80	65%	48	91.67%
Cervical mobility	80	12.50%	-	-
Thoracic mobility	80	10%	-	-
Cervical motor control	80	25%	-	-
Posture	80	13.75%	-	-
Radiating pain below elbow	80	30%	-	-
Accompanying headache	80	36.25%	-	-
Dizziness	80	18.75%	-	-
Pressure sensitivity neck musculature	80	25%	-	-
Prior conditions				
Neck pain before**	70	92.86%	-	-
History of musculoskeletal pain*	70	72.86%	-	-
General factors				
Physical inactivity**	71	90.14 %	-	-
Unhealthy lifestyle (smoking, alcohol, eating etc.)*	71	76.06%	-	-
Sleep quality*	71	73.24%	-	-

Table 3.2 continues on next page.

Table 3.2: Continued

Prognostic factors	Number of participants per factor Round 1	Percentage agreement (yes) Round 1	Number of participants per factor Round 2	Percentage Agreement (yes) Round 2
Cognition				
Somatization**	74	62.16%	48	89.58%
Catastrophizing**	74	87.84%	-	-
Locus of control	74	59.46%	-	-
Acceptance of illness	74	52.70%	-	-
Illness beliefs about recovery**	74	83.78%	-	-
Treatment beliefs*	74	70.27%	-	-
Emotions				
Depression**	72	87.50%	-	-
Kinesiophobia**	72	86.11%	-	-
Distress*	72	72.22%	-	-
Anger	72	43.06%	-	-
Injustice	72	40.28%	-	-
Behavior				
Coping**	70	95.71%	-	-
Perceptions				
Illness beliefs about pain identity**	56	89.29%	-	-
Hypervigilance *	56	76.79%	-	-
Motivation				
Purposeful behavior**	32	90.63%	-	-
Vulnerability				
Limited health literacy **	62	62.90%	48	87.50%
Limited self-regulation	62	50%	-	-
Limited self-efficacy**	62	88.71%	-	-
Remaining factors				
Health care provider attitude (biomedical/biopsychosocial)**	65	90.77%	-	-
Therapeutic relation**	65	84.62%	-	-
Additional factors round 2				
Orofacial pain	-	-	40	65%
Potential to self-modify posture**	-	-	40	82.50%

Factors with an agreement > 70% shown in bold (* > 70% agreement, ** > 80% agreement). Factors shown in italics were found not unambiguous and were asked to clarify in the second-round questionnaire.

Table 3.3: Demographics of participants at the Delphi survey

	Delphi-participants in Round 1 (185 eligible candidates invited, response N = 83, response rate 45%)	Delphi-participants Round 2 (81 participants invited*, response N = 54, response rate 67%)
Gender	Male = 56% Female = 44%	Male = 59% Female = 41%
Country of residence	The Netherlands = 30 Belgium = 18 Saudi Arabia = 2 Canada = 5 Australia = 3 Sweden = 2 Switzerland = 3 Brazil = 1 France = 1 UK = 2 South – Africa = 1 Italy = 2 Thailand = 1 Spain = 1 Norway = 1 USA = 1 Portugal = 2 New-Zealand = 1 Denmark = 1 Not given = 2	The Netherlands = 24 Belgium = 10 Saudi Arabia = 1 Canada = 2 Australia = 2 Sweden = 1 Switzerland = 3 France = 1 UK = 2 South – Africa = 1 Italy = 1 Thailand = 1 Spain = 1 USA = 1 Portugal = 1 New-Zealand = 1 Denmark = 1
Specialization	Researcher, specialization neck or chronic pain = 42 Physiotherapist = 18 Physiotherapist in Mental Health = 3 Orthopedic Manual physiotherapist = 10 Psychologist = 1 Epidemiologist = 8 Not given = 1	Researcher, specialization neck or chronic pain = 26 Physiotherapist = 14 Physiotherapist in Mental Health = 2 Orthopedic Manual physiotherapist = 7 Epidemiologist = 6

* Two participants did not leave their email address, therefore we could only invite 81 participants instead of the 83 responders in the first round.

All the potential prognostic factors to reconsider in the second round; pain intensity at baseline, high severity of experienced disability, somatization, and limited health literacy, now reached consensus (> 80%). The additional factors, orofacial pain and potential to self-modify posture, reached a 65% and 82.5% agreement score, respectively.

Table 3.4: Delphi survey round 1 Consensus agreement modifiability prognostic factors

Prognostic factors	Number of participants* Round 1	Percentage agreement (yes) Round 1	Number of participants* Round 2	Percentage agreement (yes) Round 2
Social demographic				
Gender	X	X	-	-
Age	X	X	-	-
Social class	X	X	-	-
Education level	X	X	-	-
Marital status	x	X	-	-
Work-related factors				
Employment status	42	45.24%	-	-
Happiness in work	67	71.64%	-	-
Physical work	12	75%	-	-
Symptoms				
Pain intensity at baseline	51	70.59%	42	69.05%
Duration of the neck pain	X	X	-	-
Disturbed sleep due to neck pain	46	95.65%	-	-
Reported pain in different body regions	X	X	-	-
High severity of disability	41	95.12%	-	-
High severity of experienced disability	51	94.12%	38	92.11%
Cervical mobility	8	100%	-	-
Thoracic mobility	7	100%	-	-
Cervical motor control	19	100%	-	-
Posture	10	100%	-	-
Radiating pain below elbow	24	91.67%	-	-
Accompanying headache	28	92.86%	-	-
Dizziness	15	80%	-	-
Pressure sensitivity neck musculature	20	95%	-	-
Prior conditions				
Neck pain before	X	X	-	-
History of musculoskeletal pain	X	X	-	-
General factors				
Physical inactivity	64	100%	-	-
Unhealthy lifestyle (smoking, alcohol, eating etc.)	54	88.89%	-	-
Sleep quality	52	88.46%	-	-

Table 3.4 continues on next page.

Table 3.4: Continued

Prognostic factors	Number of participants* Round 1	Percentage agreement (yes) Round 1	Number of participants* Round 2	Percentage agreement (yes) Round 2
Cognition				
Somatization	46	82.61%	43	93.02%
Catastrophizing	65	90.77%	-	-
Locus of control	44	97.73%	-	-
Acceptance of illness	39	92.31%	-	-
Illness beliefs about recovery	62	98.39%	-	-
Treatment beliefs	52	100%	-	-
Emotions				
Depression	63	76.19%	-	-
Kinesiophobia	62	98.39%	-	-
Distress	52	98.08%	-	-
Anger	31	70.97%	-	-
Injustice	29	68.97%	-	-
Behavior				
Coping	67	95.52%	-	-
Perceptions				
Illness beliefs about pain identity	50	98%	-	-
Hypervigilance	43	90.70%	-	-
Motivation				
Purposeful behavior	32	86.21%	-	-
Vulnerability				
Limited health literacy	38	71.05%	42	80.95%
Limited self-regulation	31	77.42%	-	-
Limited self-efficacy	54	94.44%	-	-
Remaining factors				
Health care provider attitude (biomedical/ biopsychosocial)	58	93.10%	-	-
Therapeutic relation	55	92.73%	-	-
Additional factors round 2				
Orofacial pain	-	-	26	73.08%
Potential to self-modify posture	-	-	29	87.88%

* Only the participants who considered these factors of prognostic value had to vote for modifiability. X Not relevant to ask for modifiability in the survey.

The workgroup concluded that the factors *bad sleep quality* and *happiness at work* are ambiguous. For this reason, the workgroup decided to perform a topical survey to get a clear view of the meaning of these factors. We asked the participants in the second-round to describe in a few sentences (1) what they consider to be ‘bad sleep quality’ and how they would measure this factor in practice, and (2) what they think we measure when we ask patients the following question: ‘*On a numeric rating scale from 0 to 10, how satisfied are you with your work? (0 = not satisfied at all, 10 = totally satisfied)*’.

Regarding sleep quality, seven themes were often mentioned: waking up several times per night (52% of the 48 participants who answered these additional questions), waking up unrefreshed (38%), sleep duration or not enough hours (< 6 hours) (35%), difficulties falling asleep (31%), not spending an appropriate amount of time in each of the sleeping phases (15%) and waking up early (8%).

Regarding happiness at work, most the participants reported: “*it is a very broad question*” and “*satisfaction with work is not equivalent or the same construct as happiness*”. The participants indicated a total of 30 themes covered in the concept “happiness at work” (e.g. work-related stress, salary aspects, success, balance life/work and the content of work).

In conclusion, both the prognostic factor ‘sleep quality’ and ‘happiness at work’ are covering different concepts, and must, therefore, be measured in more detail.

Discussion

Main findings

Following an expert meeting (m-NGT) and a two-round Delphi survey, the expert panel reached consensus (> 70%) on the following factors to be potentially prognostic of developing chronic neck pain: pain intensity at baseline, happiness in work, high severity of experienced disability, duration of neck pain, reported pain in different body regions, neck pain before, history of musculoskeletal pain, physical inactivity, limited health literacy, unhealthy lifestyle, sleep quality, catastrophizing, illness beliefs about recovery, pain identity and treatment, depression, kinesiophobia, distress, coping, hypervigilance, purposeful behavior, potential to self-modify posture, somatization, limited self-efficacy, health care provider attitude and therapeutic relations. The experts participating in the Delphi found 19 out of these 25 factors to be modifiable by physiotherapists.

Comparison with previous studies

The results of this study are in line with other prognostic research in musculoskeletal pain. In particular, psychological factors appear of important prognostic value. Psychological stress, fear avoidance beliefs, and catastrophizing were found to be associated with chronic idiopathic, non-traumatic neck.^{15–17} Whereas depressive symptoms, coping, distress and catastrophizing were found to be prognostic for chronification of low back pain.^{11–14} The findings of these studies cannot be simply generalized to patients with idiopathic nonspecific, non-traumatic, acute or subacute neck pain because these factors have never been properly investigated in this population.

Strengths and limitations methodology

We conducted two modified consensus methods to answer our research question. Researchers often begin with a local NGT to generate items that are later used in an international Delphi survey. A classic Delphi survey and the NGT Technique follow a prescribed set of procedures that reflect both behavioral and statistical processes.^{21,33} We conducted modified NGT and Delphi techniques, as research suggests that it is important to move away from the use of labels and move toward a comprehensive description of the steps taken in a specific study. We followed a prescribed method on our m-NGT and Delphi to maintain the balanced participation of our participants and the consideration of different perspectives during the process.

Limitations of the NGT method is the potential for dominant participants to unduly influence the group.²² However, in our study, this was not the case. Ranking the generated ideas is one of the key stages in an NGT. Since our preliminary aim was to explore potential prognostic factors for an international Delphi, we considered the ranking stage not applicable.²²

In order to maintain the rigor of a Delphi technique, a response rate of 70% of invited participants is recommended. Although we did not reach this rate, in neither round was there a lack of participation from a select group based on professional background or geographic area, thus excluding non-response bias.

There is a wide variation in numbers of participants in Delphi studies, according to the scope of the problem and resources available. Although there is little empirical evidence on the effect of the number of participants on the reliability or validity of consensus processes, Murphy et al. suggest that the reliability of a composite

judgement increases in the number of judges.^{33,34} Given the large number of participants and the mix of professional backgrounds involved in both rounds, we assert the sample was representative for a valid outcome of this study.

An important strength of our study is that we used purposive sampling in our m-NGT and Delphi. It is suggested that a heterogeneous group produces a higher proportion of high quality, highly acceptable solutions or recommendations than homogeneous group.²³ In our Delphi study, geographic heterogeneity was not reached. However, heterogeneity was reached in credentials, clinical experience, scientific expertise, specialization and occupation. Our research goal was to generate input for our prognostic study that is explicitly relevant for clinicians. Therefore, we deem the inclusion of both researchers and clinicians in our m-NGT and Delphi study as particularly representative for clinicians, our main focus group.

The first round of our Delphi questionnaire was structured and did not provide the possibility of much open response. It has commonly been assumed that open-ended questions would give the participant the freedom to elaborate on the topic under investigation and may increase the richness of the data collected. However, our first round was based on our systematic review, m-NGT and workgroup meetings, and therefore we believed that a large number of open-ended questions was not necessary. Nevertheless, the role of subjectivity of items supplied by the researchers in the first round could still be questioned.

Interpretation of findings

Some of our findings must be interpreted with caution because they are likely an overestimation of the degree of consensus. For example, in the second Delphi round we found remarkable high agreement scores (87.5% to 91.7%) for some factors. There are several reasons for this. First, as it is common in Delphi studies, participants had the opportunity to revise their opinion on prognostic factors that did not reach consensus in the first place. While this is usually done for all factors that failed to reach consensus, participants only had to reconsider factors with an original agreement score between 60 to 70%.²⁵ Second, the high agreement scores might be a result of participants with minority opinions dropping out.³⁵ Third, participants might have become fatigued of an additional round and agreed to end the process.²⁷

Unanimous agreement scores were found on the modifiability of some potentially prognostic factors. A reason could be that we only discussed the modifiability

with the participants who found these factors to be prognostic. These agreement scores are based on a much lower number of participants compared to the scores for prognostic value. Besides, it is likely that participants who did not agree on the prognostic value of these factors also graded these factors as not modifiable.

Clinical message and future directions

Twelve out of 25 of our potential prognostic factors and six out of 13 categories are of psychological nature, and hence, are either likely highly correlated³⁶ and/or do likely have (a) common underlying, or at least partly overlapping construct(s). This may result in different interpretations of these factors/categories across participants, potentially biasing the results of our study. In consequence, we call for greater clarity on the relatedness of psychological constructs. Further prognostic research needs to take the interaction and moderation effect of these psychological factors into account when interpreting their results.^{14,36}

Based on our findings a biopsychosocial view on patients with nonspecific acute and subacute, non-traumatic, neck pain seems to be important. It is known that physiotherapists only partially recognize the need to address the psychosocial obstacles to recovery.^{37,38} Some of these factors are considered to be modifiable by physiotherapy intervention. It is known that physiotherapists feel often unprepared to treat these obstacles.³⁸ Consequently, whether these factors are modifiable will strongly depend on the skills of the physiotherapist. Therefore, there is a need for adequate education in the knowledge of assessing and acquiring treatment skills to incorporate the psychosocial domain in patient care.³⁹

Conclusion

Following an expert meeting (m-NGT) and a two-round Delphi survey, the expert panel reached consensus (> 70%) on 25 factors. Nineteen out of these 25 factors were found to be modifiable by the experts participating in the Delphi. Most of these factors were psychological factors.

Abbreviations

m-NGT = Modified Nominal Group Technique, NVMETC = 'Nederlandse Vereniging voor Medische Ethische Toetsingscommissies' (In English: Dutch Association of Medical Research Ethics Committees), MV = Martine Verwoerd, HW = Harriet Wittink, FM = Francois Maissan, ER = Edwin de Raaij, RS = Rob Smeets.

Declarations

Ethics approval and consent to participate

Ethical approval and consent to participate in our Delphi and expert meeting was not required by the Dutch Association of Medical Research Ethics Committees (NVMETC in Dutch: 'Nederlandse Vereniging voor Medische Ethische Toetsingscommissies') because this study does not report identifiable patient's material or identifiable data.

We informed and guaranteed the participants in our expert meeting and Delphi study that their responses are treated completely anonymous. Participation was voluntary and the participants of our expert meeting signed an informed consent.

Consent for publication

Not applicable.

Availability of data and materials

The datasets used and analyzed during the current study are available from the corresponding author on reasonable request.

Competing interests

The authors declare that they have no competing interests.

Funding

This research was partly supported by the Institute of Movement studies and partly by a research voucher by Utrecht University of Applied Sciences. The funders had no role in study design, data collection and analysis, decision to publish, or preparation of the manuscript.

Authors' contributions

All authors materially participated in this research. Their main contribution to the manuscript is described below:

Miss M.J. Verwoerd and dr. H. Wittink: substantial contribution to study conception; study design, data analysis, data interpretation, drafting and revising the manuscript; Mr. F. Maissan: contribution to study conception, data analysis, data

interpretation, drafting and revising the manuscript; Prof. dr. R.J.E.M. Smeets: contribution to study conception, data analysis, data interpretation, drafting and revising the manuscript.

Acknowledgements

We would like to thank all the healthcare professionals and researchers who have participated in this research. In particular, all the experts who gave their free time participating in the expert meeting and to respond to our Delphi survey.

We would also wish to extend our special thanks to Edwin de Raaij and Stefan Elbers, Utrecht University of Applied Sciences, for their helpful contribution during our workgroup meeting.

References

1. Childs JD, Cleland JA, Elliott JM, Teyhen DS, Wainner RS, Whitman JM, et al. Neck Pain: Clinical practice guidelines linked to the international classification of functioning, disability, and health from the orthopedic section of the american physical therapy association. *J Orthop Sport Phys Ther.* 2008;38:A1–34. doi:10.2519/jospt.2008.0303.
2. Hush JM, Lin CC, Michaleff ZA, Verhagen A, Refshauge KM. Prognosis of Acute Idiopathic Neck Pain is Poor: A Systematic Review and Meta-Analysis. *YAPMR.* 2011; 92:824–9. doi:10.1016/j.apmr.2010.12.025.
3. Vos CJ, Verhagen AP, Passchier J, Koes BW. Clinical course and prognostic factors in acute neck pain: An inception cohort study in general practice. *Pain Med.* 2008;9:572–80.
4. Koppes D. Zorg voor de fysiotherapeut - top-10 gezondheidsproblemen (DCSPH). Nivel. Accessed 7. <http://www.nivel.nl/node/4677>.
5. Geneen LJ SB, Andrew Moore R, Clarke C, Martin D, Colvin LA, Smith BH. Cochrane Database of Systematic Reviews Physical activity and exercise for chronic pain in adults: an overview of Cochrane Reviews (Review) Physical activity and exercise for chronic pain in adults: an overview of Cochrane Reviews (Review) i Physical acti. *Cochrane Database Syst Rev.* 2017. doi:10.1002/14651858.CD011279.pub3.
6. Bertozzi L, Gardenghi I, Turoni F, Villafañe JH, Capra F, Guccione AA, et al. Effect of Therapeutic Exercise on Pain and Disability in the Management of Chronic Nonspecific Neck Pain: Systematic Review and Meta-Analysis of Randomized Trials. *Phys Ther.* 2013; 93:1026–36.
7. Gross A, Langevin P, Burnie SJ, Bédard-Brochu M-S, Empey B, Dugas E, et al. Manipulation and mobilisation for neck pain contrasted against an inactive control or another active treatment. *Cochrane Database Syst Rev.* 2015;23. doi:10.1002/14651858.CD004249.pub4.
8. Verwoerd M, Wittink H, Maissan F, de Raaij E, Smeets RJEM. Prognostic factors for persistent pain after a first episode of nonspecific idiopathic, non-traumatic neck pain: A systematic review. *Musculoskelet Sci Pract.* 2019;42 March 2018:13–37. doi:10.1016/j.msksp.2019.03.009.
9. Walton DM. 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.
10. Artus M, Campbell P, Mallen CD, Dunn KM, Van Der Windt DAW. Generic prognostic factors for musculoskeletal pain in primary care: a systematic review. *BMJ Open.* 2017;7. doi:10.1136/.
11. Wertli MM, Rasmussen-Barr E, Weiser S, Bachmann LM, Brunner F. The role of fear avoidance beliefs as a prognostic factor for outcome in patients with nonspecific low back pain: A systematic review. *Spine J.* 2014;14:816–36. doi:10.1016/j.spinee.2013.09.036.
12. Wertli MM, Eugster R, Held U, Steurer J, Kofmehl R, Weiser S. Catastrophizing - A prognostic factor for outcome in patients with low back pain: A systematic review. *Spine J.* 2014;14:2639–57. doi:10.1016/j.spinee.2014.03.003.
13. George SZ, Beneciuk JM. Psychological predictors of recovery from low back pain: A prospective study. *BMC Musculoskelet Disord.* 2015;16:1–7.
14. Nicholas MK, Linton SJ, Watson PJ, Main CJ. Early Identification and Management of Psychological Risk Factors (“Yellow Flags”) in Patients With Low Back Pain: A Reappraisal. *Phys Ther.* 2011;91:737–53. doi:10.2522/ptj.20100224.

15. Ortego G, Villafaña JH, Doménech-García V, Berjano P, Bertozzi L, Herrero P. Is there a relationship between psychological stress or anxiety and chronic nonspecific neck-arm pain in adults? A systematic review and meta-analysis. *J Psychosom Res.* 2016;90:70–81. doi:10.1016/j.jpsychores.2016.09.006.
16. Thompson DP, Urmston M, Oldham JA, Woby SR. The association between cognitive factors, pain and disability in patients with idiopathic chronic neck pain. *Disabil Rehabil.* 2010;32:1758–67.
17. 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;13:239–48.
18. Wingbermühle RW, van Trijffel E, Nelissen PM, Koes B, Verhagen AP. Few promising multivariable prognostic models exist for recovery of people with non-specific neck pain in musculoskeletal primary care: a systematic review. *J Physiother.* 2018;64:16–23.
19. Kelly J, Ritchie C, Sterling M. Clinical prediction rules for prognosis and treatment prescription in neck pain: A systematic review. *Musculoskelet Sci Pract.* 2017;27:155–64.
20. Turk DC OA. Psychological Factors in Chronic Pain: Evolution and Revolution. *J Consult Clin Psychol.* 2002;70:678.
21. Jones J, Hunter D. Qualitative Research: Consensus methods for medical and health services research. *Bmj.* 1995;311:376.
22. Humphrey-Murto S, Varpio L, Gonsalves C, Wood TJ. Using consensus group methods such as Delphi and Nominal Group in medical education research*. *Med Teach.* 2017; 39:14–9.
23. Delbecq, Andre L, Van de Ven, Andrew H., Gustafson D. Group Techniques for Program Planning; a guide to nominal group and Delphi processes. 1975.
24. Millar K. Ethical Delphi Manual. 2006; February.
25. McMillan SS, King M, Tully MP. How to use the nominal group and Delphi techniques. *Int J Clin Pharm.* 2016;38:655–62.
26. Hasson F, Keeney S, McKenna H. Research guidelines for the Delphi survey technique. *J Adv Nurs.* 2000;32:1008–15.
27. Keeney S, Hasson F, McKenna H. Consulting the oracle: Ten lessons from using the Delphi technique in nursing research. *J Adv Nurs.* 2006;53:205–12.
28. Fraser C Ferguson, Margaret Brownlee, Valerie W. A Delphi study investigating consensus among expert physiotherapists in relation to the management of low back pain. *Musculoskeletal Care.* 2008;6:197–210.
29. Vogel C, Zwolinsky S, Griffiths C, Hobbs M, Henderson E, Wilkins E. A Delphi study to build consensus on the definition and use of big data in obesity research. *Int J Obes.* 2019;43:2573–86.
30. Slade SC, Dionne CE, Underwood M, Buchbinder R. Standardised method for reporting exercise programmes: Protocol for a modified Delphi study. *BMJ Open.* 2014;4:1–5.
31. Henderson EJ, Rubin GP. Development of a community-based model for respiratory care services. *BMC Health Serv Res.* 2012;12:1–10.
32. Al Juffali LA, Knapp P, Al-Aqeel S, Watson MC. Medication safety problems priorities in community pharmacy in Saudi Arabia: A multi-stakeholder Delphi study using the human factors framework. *BMJ Open.* 2019;9:1–10.
33. Catherine P. The Delphi technique: myths and realities. *J Adv Nurs.* 2003;41:376–82. <http://www.embase.com/search/results?subaction=viewrecord&from=export&id=L36478234>.

34. Murphy E, Dingwall R, Greatbatch D, Parker S, Watson P. Qualitative research methods in health technology assessment: A review of the literature. *Health Technol Assess (Rockv)*. 1998;2.
35. Bardecki MJ. Participants' response to the Delphi method: An attitudinal perspective. *Technol Forecast Soc Change*. 1984;25:281–92.
36. Campbell P, Bishop A, Dunn KM, Main CJ, Thomas E, Foster NE. Conceptual overlap of psychological constructs in low back pain. *Pain*. 2013;154:1783–91.
37. Sanders T, Foster NE, Bishop A, Ong BN. Biopsychosocial care and the physiotherapy encounter: Physiotherapists' accounts of back pain consultations. *BMC Musculoskelet Disord*. 2013;14.
38. Synnott A, O'Keeffe M, Bunzli S, Dankaerts W, O'Sullivan P, O'Sullivan K. Physiotherapists may stigmatise or feel unprepared to treat people with low back pain and psychosocial factors that influence recovery: A systematic review. *J Physiother*. 2015;61:68–76. doi:10.1016/j.jphys.2015.02.016.
39. Alexanders J, Anderson A, Henderson S. Musculoskeletal physiotherapists' use of psychological interventions: A systematic review of therapists' perceptions and practice. *Physiother (United Kingdom)*. 2015;101:95–102.

Appendix 3.1: Delphi Questionnaire round 1

Prognostic factors for persistent pain after a first episode of nonspecific idiopathic, non-traumatic neck pain.

A Delphi Study



Prognostic factors for persistent pain after a first episode of nonspecific idiopathic, non-traumatic neck pain.

A Delphi Study

We would like to invite you to participate in a Delphi study at the University of Applied Sciences Utrecht in collaboration with Maastricht University (department Rehabilitation Medicine).

We recently conducted a systematic review of the literature regarding prognostic factors of acute and subacute, non-traumatic, neck pain for chronification. The review reveals that it is still unclear which factors are prognostic for chronification of acute and subacute neck pain. To prevent chronic neck pain, and to specifically intervene on modifiable prognostic factors, more research is important.

We are therefore starting a longitudinal prognostic cohort study to acquire more knowledge in this area. Within this study, we will focus on prognostic factors that are modifiable by a physiotherapist; we will not focus on risk factors or predictive factors (see below for our definitions).

To create a list of potential and relevant prognostic factors, we would like to invite you to participate as an expert in this Delphi Study. We have invited scientists, practicing GP's, physiotherapists with different specializations, remedial therapists and other health care providers to participate in the Delphi Study.

The design of our Delphi Study is as follows. In the first round, and based on your input, we will send out a questionnaire to experts in the field. The responses will then be analyzed. In the second round, and based on our analysis, we will send out a follow-up questionnaire. This procedure will be repeated until consensus is reached, or until no new information emerges. The questionnaire will consist of a number of open and a number of closed questions.

We would be very grateful if you could find some time to participate in this Delphi Study. Completing this questionnaire takes around 10-15 minutes.

If you have any questions or want further information, please do not hesitate to contact Martine Verwoerd (martine.verwoerd@hu.nl).

Thank you very much for your time.

Yours sincerely,

Martine Verwoerd PT
Harriet Wittink PhD PT
Francois Maissan MSc
Professor Rob Smeets PhD MD

“Definitions”:

Prognostic factors are factors that influence the natural course of a disease in patients. Prognostic factors concern patients that suffer from acute or subacute neck pain, and who need care for their acute or subacute, non-traumatic, neck pain by a physiotherapist.

Predictive factors are defined as characteristics that identify subgroups of treated patients having different outcomes and can be used to help predict whether a person’s neck pain will respond to a specific treatment. Before clinical characteristics can be used to justify specific treatments, it is imperative that the prognostic effects of these characteristics are distinguished from their ability to predict a differential clinical benefit from a specific treatment.

Risk factors are factors that increase the risk of developing a disease. Risk factors concern people who do not suffer from acute or subacute neck pain yet, and who therefore do not need care by a physiotherapist yet. In our study, we are not looking for risk factors.

Acute, subacute and chronic pain are conform the definition of the ICD-11: acute pain has a duration of 0-2 weeks; subacute pain has a duration of 2 weeks to 3 months; chronic pain has a duration of more than 3 months, or is pain with a recurrent character.

We guarantee that your answers are treated completely anonymous.

To allow follow-up questions and to get some demographic statistics about the respondents of our study, please provide us with some personal details.

Name:

E-mail address:

Country:

Specialisation or expertise:

We have identified 12 different categories of prognostic factors. In the following pages, we will present you a list of factors separately for each category. We start with the "social demographic" category on this page.

Please indicate for each factor whether you consider this factor as a prognostic factor for chronification in patients with acute or subacute, non-traumatic, neck pain.

In case you consider a factor as prognostic, please also indicate whether you expect this factor to be modifiable by a physiotherapeutic intervention and how we should measure the factor in practice.

If you think that some prognostic factors are missing on our lists, please write them down under the bullet point "Alternative".

To give an example:

Prior research shows that low back pain at the start of the first episode of neck pain is a prognostic factor for chronification of the neck pain. Please ask yourself whether indeed lower back pain is the prognostic factor, or whether there is an underlying factor (or factors) that has an impact on both low back pain and neck pain.

Category: Social demographic

☐ Gender

☐ Age

☐ Social class

☐ Education level

☐ Marital status

☐ Alternative:

Is 'your alternative' modifiable? ☐ Yes ☐ No

How would you measure this factor in clinical practice?

Please indicate for each factor whether you consider this factor as a prognostic factor for chronification in patients with acute or subacute, non-traumatic, neck pain.
In case you consider a factor as prognostic, please indicate whether you expect this factor to be modifiable by a physiotherapeutic intervention and how we should measure the factor in practice.

Category: Work-related factors

☐ Employment status

☐ Happiness in work

☐ Physical work

☐ Alternative:

Is 'Employment status' modifiable? Yes ☐ No ☐

How would you measure this factor in clinical practice?

Is 'Happiness in work' modifiable? Yes ☐ No ☐

How would you measure this factor in clinical practice?

Is 'Physical work' modifiable? Yes ☐ No ☐

How would you measure this factor in clinical practice?

Is 'your alternative' modifiable? Yes ☐ No ☐

How would you measure this factor in clinical practice?

Please indicate for each factor whether you consider this factor as a prognostic factor for chronification in patients with acute or subacute, non-traumatic, neck pain.

In case you consider a factor as prognostic, please indicate whether you expect this factor to be modifiable by a physiotherapeutic intervention and how we should measure the factor in practice.

Category: Symptoms

- ☐ Pain intensity at baseline
- ☐ Duration of the neck pain
- ☐ Disturbed sleep due to neck pain
- ☐ Reported pain in different body regions
- ☐ High severity of disability
- ☐ High severity of experienced disability (ability)
- ☐ Cervical mobility
- ☐ Thoracic mobility
- ☐ Cervical motor control
- ☐ Posture
- ☐ Radiating pain below elbow
- ☐ Accompanying headache
- ☐ Dizziness
- ☐ Pressure sensitivity neck musculature
- ☐ Alternative:

Is 'pain intensity at baseline modifiable?' Yes ☐ No ☐

How would you measure this factor in clinical practice?

Is 'disturbed sleep due to neck pain' modifiable? Yes ☐ No ☐

How would you measure this factor in clinical practice?

Is 'high severity of disability' modifiable? Yes ☐ No ☐

How would you measure this factor in clinical practice?

Is 'high severity of experienced disability' modifiable? Yes ☐ No ☐

How would you measure this factor in clinical practice?

Is 'cervical mobility' modifiable? Yes ☐ No ☐

How would you measure this factor in clinical practice?

Is 'cervical motor control' modifiable? Yes ☐ No ☐

How would you measure this factor in clinical practice?

Is 'posture' modifiable? Yes ☐ No ☐

How would you measure this factor in clinical practice?

Is 'radiating pain below elbow' modifiable? Yes ☐ No ☐

How would you measure this factor in clinical practice?

Is 'accompanying headache' modifiable? Yes ☐ No ☐

How would you measure this factor in clinical practice?

Is 'dizziness' modifiable? Yes ☐ No ☐

How would you measure this factor in clinical practice?

Is 'pressure sensitivity neck musculature' modifiable? Yes ☐ No ☐

How would you measure this factor in clinical practice?

Is 'your alternative' modifiable? Yes ☐ No ☐

How would you measure this factor in clinical practice?

Please indicate for each factor whether you consider this factor as a prognostic factor for chronification in patients with acute or subacute, non-traumatic, neck pain.

In case you consider a factor as prognostic, please indicate whether you expect this factor to be modifiable by a physiotherapeutic intervention and how we should measure the factor in practice.

Category: Prior conditions

Neck pain before

History of musculoskeletal pain

Alternative:

Is 'your alternative' modifiable? Yes ☐ No ☐

How would you measure this factor in clinical practice?

Please indicate for each factor whether you consider this factor as a prognostic factor for chronification in patients with acute or subacute, non-traumatic, neck pain.

In case you consider a factor as prognostic, please indicate whether you expect this factor to be modifiable by a physiotherapeutic intervention and how we should measure the factor in practice.

Category: General health

☐ Physical inactivity

☐ Unhealthy lifestyle (smoking, alcohol, eating etc.)

☐ Sleep quality

☐ Alternative:

Is 'physical inactivity' modifiable? Yes ☐ No ☐

How would you measure this factor in clinical practice?

Is 'unhealthy lifestyle' modifiable? Yes ☐ No ☐

How would you measure this factor in clinical practice?

Is 'sleep quality' modifiable? Yes ☐ No ☐

How would you measure this factor in clinical practice?

Is 'your alternative' modifiable? Yes ☐ No ☐

How would you measure this factor in clinical practice?

The following categories focus more on **psychological factors**. Since assigning factors to a specific "psychological" category involves judgement, please indicate in the following text box whether you think that a certain factor better belongs to another category.

For your overview, here is the list of all categories that focus on psychological factors:
Cognition, Emotions, Behavior, Perceptions, Motivation, Vulnerability.

Please indicate for each factor whether you consider this factor as a prognostic factor for chronification in patients with acute or subacute, non-traumatic, neck pain.
In case you consider a factor as prognostic, please indicate whether you expect this factor to be modifiable by a physiotherapeutic intervention and how we should measure the factor in practice.

Category: Cognition

- ☐ Somatization
- ☐ Catastrophizing
- ☐ Locus of control
- ☐ Acceptance of illness
- ☐ Illness beliefs about recovery
- ☐ Treatment beliefs
- ☐ Alternative:

Explanation prognostic factors

Somatization: when physical symptoms are caused by psychological or emotional factors.

Catastrophizing: an exaggerated negative orientation towards a negative stimuli. This makes catastrophizing a cognitive phenomenon.

Locus of control: this can be internal or external control. Internal control: the extent to which the patient thinks he/she can control the pain. External control: the extent to which the patient thinks that other people can control his/her pain.

Treatment beliefs: this includes the patient's beliefs about how treatment may help to control or recover from the illness.

Is 'somatization' modifiable? Yes ☐ No ☐

How would you measure this factor in clinical practice?

Is 'catastrophizing' modifiable? Yes ☐ No ☐

How would you measure this factor in clinical practice?

Is 'locus of control' modifiable? Yes ☐ No ☐

How would you measure this factor in clinical practice?

Is 'acceptance of illness' modifiable? Yes ☐ No ☐

How would you measure this factor in clinical practice?

Is 'illness beliefs about recovery' modifiable? Yes ☐ No ☐

How would you measure this factor in clinical practice?

Is 'treatment beliefs' modifiable? Yes ☐ No ☐

How would you measure this factor in clinical practice?

Is 'your alternative' modifiable? Yes ☐ No ☐

How would you measure this factor in clinical practice?

The following categories focus more on **psychological factors**. Since assigning factors to a specific "psychological" category involves judgement, please indicate in the following text box whether you think that a certain factor better belongs to another category.

For your overview, here is the list of all categories that focus on psychological factors:
Cognition, Emotions, Behavior, Perceptions, Motivation, Vulnerability.

Please indicate for each factor whether you consider this factor as a prognostic factor for chronification in patients with acute or subacute, non-traumatic, neck pain.
In case you consider a factor as prognostic, please indicate whether you expect this factor to be modifiable by a physiotherapeutic intervention and how we should measure the factor in practice.

Category: Emotions

- ☐ Depression
- ☐ Kinesiophobia
- ☐ Distress
- ☐ Anger
- ☐ Injustice
- ☐ Alternative:

Explanation prognostic factors

Depression: condition that comes under 'mental illness'. There is a depressive mood when there is an abnormal depression for a longer period (longer than two weeks) and/or an abnormal lethargy, loss of interest or an inability to enjoy something. We mean both light and heavier depressions.

Kinesiophobia: fear of movement.

Distress: negative stress. This means stress that is not in the interests of a person and is experienced as a unpleasant external stimulus.

Anger: angry mood (irritability, frustration) or a negative social cognitions (interpersonal sensitivity, envy, disagreeableness).

Is 'depression' modifiable? Yes ☐ No ☐

How would you measure this factor in clinical practice?

Is 'kinesiophobia' modifiable? Yes ☐ No ☐

How would you measure this factor in clinical practice?

Is 'distress' modifiable? Yes ☐ No ☐

How would you measure this factor in clinical practice?

Is 'anger' modifiable? Yes ☐ No ☐

How would you measure this factor in clinical practice?

Is 'injustice' modifiable? Yes ☐ No ☐

How would you measure this factor in clinical practice?

Is 'your alternative' modifiable? Yes ☐ No ☐

How would you measure this factor in clinical practice?

The following categories focus more on **psychological factors**. Since assigning factors to a specific "psychological" category involves judgement, please indicate in the following text box whether you think that a certain factor better belongs to another category.

For your overview, here is the list of all categories that focus on psychological factors:
Cognition, Emotions, Behavior, Perceptions, Motivation, Vulnerability

Please indicate for each factor whether you consider this factor as a prognostic factor for chronification in patients with acute or subacute, non-traumatic, neck pain.
In case you consider a factor as prognostic, please indicate whether you expect this factor to be modifiable by a physiotherapeutic intervention and how we should measure the factor in practice.

Category: Behavior

☐ Coping

☐ Alternative:

Explanation prognostic factors

Coping: the way someone deals with problems or stress.

Is 'coping' modifiable? Yes ☐ No ☐

How would you measure this factor in clinical practice?

Is 'your alternative' modifiable? Yes ☐ No ☐

How would you measure this factor in clinical practice?

The following categories focus more on **psychological factors**. Since assigning factors to a specific "psychological" category involves judgement, please indicate in the following text box whether you think that a certain factor better belongs to another category.

For your overview, here is the list of all categories that focus on psychological factors: Cognition, Emotions, Behavior, Perceptions, Motivation, Vulnerability.

Please indicate for each factor whether you consider this factor as a prognostic factor for chronification in patients with acute or subacute, non-traumatic, neck pain.
In case you consider a factor as prognostic, please indicate whether you expect this factor to be modifiable by a physiotherapeutic intervention and how we should measure the factor in practice.

Category: Perceptions

☐ Illness beliefs about pain identity

☐ Hypervigilance

☐ Alternative:

Explanation prognostic factors

Illness beliefs about pain identity: This includes perceptions about the label or name given to the condition by patients and the symptoms that are perceived to go with it.

Hypervigilance: to pain or somatic sensations is the excessive tendency to attend to pain/somatic sensations, or the excessive readiness to select pain-related information over other information from the environment.

Is 'illness beliefs about pain identity' modifiable? Yes ☐ No ☐

How would you measure this factor in clinical practice?

Is 'hypervigilance' modifiable? Yes ☐ No ☐

How would you measure this factor in clinical practice?

Is 'your alternative' modifiable? Yes ☐ No ☐

How would you measure this factor in clinical practice?

The following categories focus more on **psychological factors**. Since assigning factors to a specific "psychological" category involves judgement, please indicate in the following text box whether you think that a certain factor better belongs to another category.

For your overview, here is the list of all categories that focus on psychological factors:
Cognition, Emotions, Behavior, Perceptions, Motivation, Vulnerability.

Please indicate for each factor whether you consider this factor as a prognostic factor for chronification in patients with acute or subacute, non-traumatic, neck pain.
In case you consider a factor as prognostic, please indicate whether you expect this factor to be modifiable by a physiotherapeutic intervention and how we should measure the factor in practice.

Category: Motivation

☐ Purposeful behavior

☐ Alternative:

Is 'purposeful behavior' modifiable? Yes ☐ No ☐

How would you measure this factor in clinical practice?

Is 'your alternative' modifiable? Yes ☐ No ☐

How would you measure this factor in clinical practice?

The following categories focus more on **psychological factors**. Since assigning factors to a specific "psychological" category involves judgement, please indicate in the following text box whether you think that a certain factor better belongs to another category.

For your overview, here is the list of all categories that focus on psychological factors: Cognition, Emotions, Behavior, Perceptions, Motivation, Vulnerability.

Please indicate for each factor whether you consider this factor as a prognostic factor for chronification in patients with acute or subacute, non-traumatic, neck pain. In case you consider a factor as prognostic, please indicate whether you expect this factor to be modifiable by a physiotherapeutic intervention and how we should measure the factor in practice.

Category: Vulnerability

☐ Limited health literacy

☐ Limited self-regulation

☐ Limited self-efficacy

☐ Alternative:

Explanation prognostic factors

Health literacy: has been defined as the cognitive and social skills which determine the motivation and ability of individuals to gain access to, understand and use information in ways which promote and maintain good health.

Self-regulation: a plan for patients to eliminate health risk behaviors. It includes self-monitoring, self-evaluation, and self-reinforcement.

Self-efficacy: confidence in ability to successfully perform specific tasks or behaviors related to one's health in a variety of situations.

Is 'limited health literacy' modifiable? Yes ☐ No ☐

How would you measure this factor in clinical practice?

Is 'limited self-regulation' modifiable? Yes ☐ No ☐

How would you measure this factor in clinical practice?

Is 'limited self-efficacy' modifiable? Yes ☐ No ☐

How would you measure this factor in clinical practice?

Is 'your alternative' modifiable? Yes ☐ No ☐

How would you measure this factor in clinical practice?

Remaining factors

☐ Health care provider attitude (biomedical/ biopsychosocial)

☐ Therapeutic relation

☐ Alternative:

Is 'health care provider attitude' modifiable? Yes ☐ No ☐

How would you measure this factor in clinical practice?

Is 'therapeutic relation' modifiable? Yes ☐ No ☐

How would you measure this factor in clinical practice?

Is 'your alternative' modifiable? Yes ☐ No ☐

How would you measure this factor in clinical practice?

Thank you very much for your participation! We highly appreciate it.

We will send you the results of this first round of our Delphi study. We will also ask you again to participate in the second round of our Delphi study.

If there is anything you would like us to know, please use the comment field below.

Appendix 3.2: Delphi Questionnaire round 2

Prognostic factors for persistent pain after a first episode of nonspecific idiopathic, non-traumatic neck pain.

A Delphi Study - Round 2



Prognostic factors for persistent pain after a first episode of nonspecific idiopathic, non-traumatic neck pain.

Second and final round Delphi Study

First of all, we are very thankful that nearly 90 experts participated in the first round of our Delphi Study. We very much appreciate your opinion and feedback. **You can find the results of the first round below.**

We now invite you to participate in the second and final round of our Delphi study.

The goal is to obtain a list of potential modifiable prognostic factors for chronification of acute and subacute neck pain (please see our definitions of terms below). This final list of factors will form the basis of the subsequent longitudinal prognostic cohort study.

The second questionnaire is significantly shorter than the first one and consists of some open and closed questions. It will take approximately 5 to 10 minutes of your time.

We would again be very grateful if you can spare some time and also participate in the final round of our Delphi Study.

If you have any questions or want further information, please do not hesitate to contact Martine Verwoerd (martine.verwoerd@hu.nl).

Thank you very much for your time.

Yours sincerely,

Martine Verwoerd PT
Harriet Wittink PhD PT
Francois Maissan MSc
Professor Rob Smeets PhD MD

"Definitions":

Acute, subacute and chronic pain are conform the definition of the ICD-11.

Acute pain has a duration of 0-2 weeks;

Subacute pain has a duration of 2 weeks to 3 months;

Chronic pain has a duration of more than 3 months, or is pain with a recurrent character.

We guarantee that your answers are treated completely anonymous.

To allow follow-up questions and to get some demographic statistics about the respondents of our study, please provide us with some personal details.

Name:

E-mail address:

Country:

Specialisation or expertise:

Second round Delphi - Part 1: Reconsider prognostic factors

There were some prognostic factors with an agreement score between 60-70%. We would like to get more input on these factors.

Prior literature considers some of the factors as prognostic for musculoskeletal pain in **other regions**. To avoid false-negative findings on such factors, can you please indicate (again) whether you consider the factors as being prognostic for chronification in patients with acute or subacute, non-traumatic **neck pain**.

If you consider this factor to be **not** prognostic for chronification of **neck pain**, can you please describe why not.

If you consider this factor to be prognostic for chronification of **neck pain**, please indicate whether you expect this factor to be modifiable by a physiotherapeutic intervention.

You find further information and definitions of our concepts by clicking on the question mark sign.

- ☐ Pain intensity at baseline
- ☐ High severity of experienced disability
- ☐ Somatization
- ☐ Limited health literacy

Is 'pain intensity at baseline' modifiable? Yes ☐ No ☐

Please describe why you consider 'pain at baseline' not as a prognostic factor.

Is 'experienced disability' modifiable? Yes ☐ No ☐

Please describe why you consider 'high severity of experienced disability' not as a prognostic factor.

Is 'somatization' modifiable? Yes ☐ No ☐

Please describe why you consider 'somatization' not as a prognostic factor.

Is 'limited health literacy' modifiable? Yes ☐ No ☐

Please describe why you consider 'limited health literacy' not as a prognostic factor.

Second round Delphi - Part 2: Additional prognostic factors

We present you some more potentially prognostic factors. Please indicate whether you consider each factor as a prognostic factor for chronification in patients with acute or subacute, non-traumatic, neck pain.

If you consider a factor as prognostic, please indicate whether you expect this factor to be **modifiable** by a physiotherapeutic intervention and how we should **measure** the factor in practice.

☐ Orofacial pain

☐ Potential to self-modify posture during work

Is 'orofacial pain' modifiable? Yes ☐ No ☐

How would you measure this factor in clinical practice?

Is 'potential to self-modify posture during work' modifiable? Yes ☐ No ☐

How would you measure this factor in clinical practice?

For two prognostic factors with overall high agreement scores we have difficulties in assessing what these factors actually mean and how we could measure them.

These factors are (1) sleep quality, and (2) happiness at work. We therefore ask you for your input.

(1) **Sleep quality:** Please describe (i) what you consider to be "bad sleep quality", and (ii) how you would measure "bad sleep quality".

(1)

(2)

(2) **Happiness at work:** We consider using the following question in our study to capture happiness at work:

"On a numeric rating scale from 0 to 10, how satisfied are you in your work? (0 = not satisfied at all, 10 = totally satisfied)"

Please tell us what comes to your mind when reading this question.

We would like you to describe in a few sentences, what you think we do exactly measure with this question?

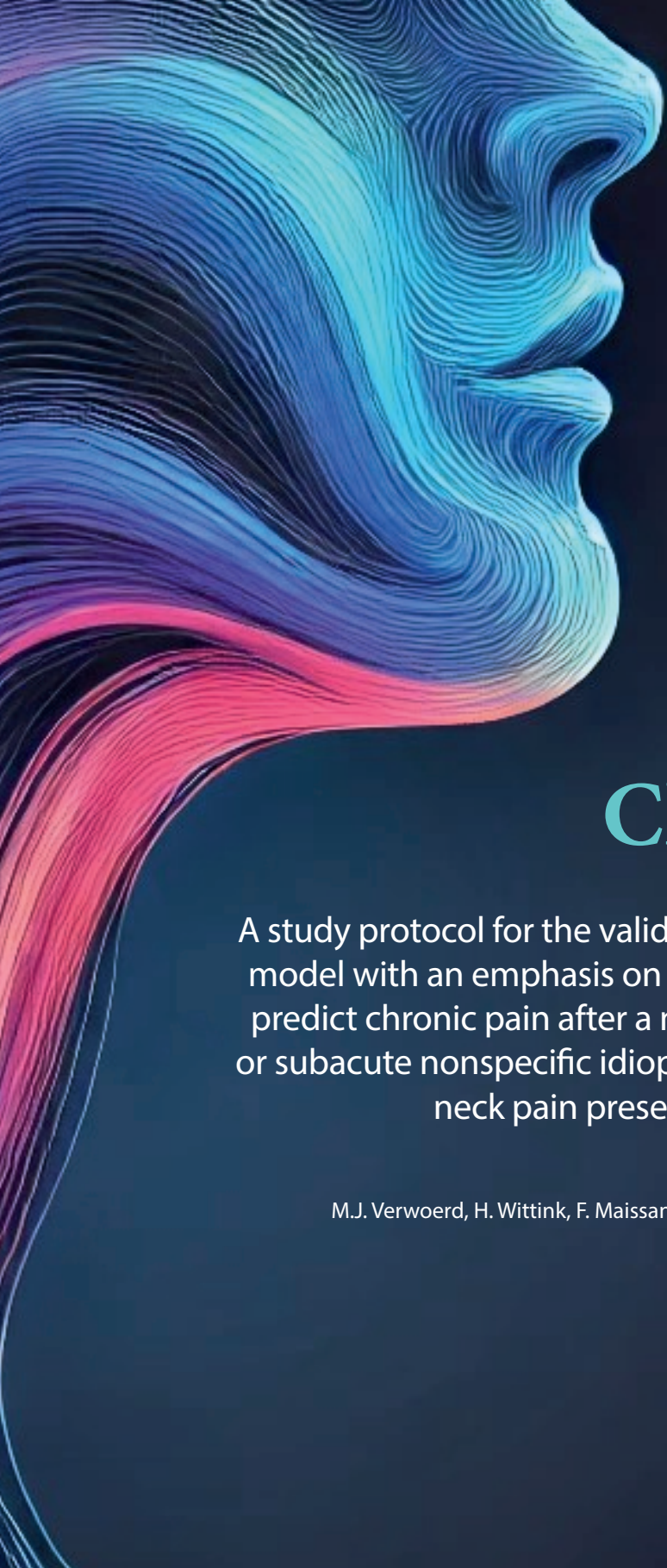
Thank you very much for your participation! We highly appreciate it.

We will send you the results of the second round of our Delphi study. We do not expect to have a third round.

If there is anything you would like us to know, please use the comment field below.

Part 2





Chapter 4

A study protocol for the validation of a prognostic model with an emphasis on modifiable factors to predict chronic pain after a new episode of acute or subacute nonspecific idiopathic, non-traumatic neck pain presenting in primary care

M.J. Verwoerd, H. Wittink, F. Maissan, S.M.J. van Kuijk, R.J.E.M. Smeets

Published PLoS One, 2023

Background: The primary objective of this study is to identify which modifiable and non-modifiable factors are independent predictors of the development of chronic pain in patients with acute or subacute nonspecific idiopathic, non-traumatic neck pain, and secondly, to combine these to develop and internally validate a prognostic prediction model.

Methods: A prospective cohort study will be conducted by physiotherapists in 30 primary physiotherapy practices between January 26, 2020, and August 31, 2022, with a 6-month follow-up until March 17, 2023. Patients who consult a physiotherapist with a new episode of acute (0 to 3 weeks) or subacute neck pain (4 to 12 weeks) will complete a baseline questionnaire. After their first appointment, candidate prognostic variables will be collected from participants regarding their neck pain symptoms, prior conditions, work-related factors, general factors, psychological and behavioral factors. Follow-up assessments will be conducted at six weeks, three months, and six months after the initial assessment.

The primary outcome measure is the Numeric Pain Rating Scale (NPRS) to examine the presence of chronic pain. If the pain is present at six weeks, three months, and six months with a score of NPRS ≥ 3 , it is classified as chronic pain.

An initial exploratory analysis will use univariate logistic regression to assess the relationship between candidate prognostic factors at baseline and outcome. Multiple logistic regression analyses will be conducted. The discriminative ability of the prognostic model will be determined based on the Area Under the receiver operating characteristic Curve (AUC), calibration will be assessed using a calibration plot and formally tested using the Hosmer and Lemeshow goodness-of-fit test, and model fit will be quantified as Nagelkerke's R². Internal validation will be performed using bootstrapping-resampling to yield a measure of overfitting and the optimism-corrected AUC.

Discussion: The results of this study will improve the understanding of prognostic and potential protective factors, which will help clinicians guide their clinical decision making, develop an individualized treatment approach, and predict chronic neck pain more accurately.

Key words: Chronification, neck pain, prognostic model, modifiable factors

Introduction

Neck pain is one of the most prevalent and disabling health conditions, with a substantial impact on public health.^{1,2} The Global Burden of Disease study demonstrated that neck pain is third in the ranking of ‘years lived with disability’ in non-fatal diseases in Europe.³ Costs related to neck pain are rising mainly due to extended work absence and usage of health care services.^{1,4,5} In particular, neck pain that becomes chronic causes high healthcare costs.⁶ The prevalence of chronic neck pain has increased from 2005 to 2015 by 21% up to approximately 358 million people worldwide, and it is likely to increase further in Western countries due to an aging population.⁷ In the Netherlands, pain in the cervical region is the most commonly reported complaint for which patients seek help in physiotherapy practices.⁸

Recovery from neck pain and related disability mainly occurs in the first few weeks. Thereafter, the recovery rate is much lower.^{9,10} The reported effect of physiotherapy treatment in patients with chronic musculoskeletal pain is, at best, only moderate.^{11–13} It is therefore not surprising that defining the natural course and the prognostic factors in people with acute and subacute neck pain is a top-five priority of the new agenda for Neck Pain Research.¹⁴ Knowledge of prognostic factors can help health care providers to improve clinical decision-making and is a likely key factor in combatting chronification of idiopathic neck pain. Preventing chronicity should be the major focus of physiotherapists in the (sub)acute phase of musculoskeletal pain. Being able to predict which patients with neck pain are likely to develop chronic pain may help prevent chronification of pain in physiotherapy practices.

At the present time the existing literature on prognostic models shows a low performance in predicting chronicity or recovery from neck pain.^{15,16} It is thereby not applicable as a starting point for a new prognostic study. A limitation and possible explanation of this low performance is the inclusion of a too-heterogeneous group of neck pain patients. Most studies include (sub)acute neck pain, whiplash-related neck pain, pain with neurological symptoms, and even patients who already have chronic pain,^{15,17,18} although these groups are known to differ in both clinical symptoms and prognosis.^{19–21} Therefore, it seems useful to pay attention to the pain etiology and pathophysiological mechanisms of the existent pain in classification and inclusion systems.²²

In addition, prognostic research has often focused on factors that are non-modifiable by physiotherapists, such as age and sex.²³ Only clinically modifiable factors have the potential to change patient outcome and are therefore recommended to be included in prognostic research.^{16,24} However, to strengthen a prognostic model, it can be relevant to include some non-modifiable factors. Based on a recent consensus study of potential modifiable prognostic factors, including psychosocial factors in prognostic research for chronification is relevant.²⁵ It seems that psychosocial factors in particular can be modified. Furthermore, it is known that neurophysiological changes in the chronification of pain are modulated by psychosocial factors.²⁶

Therefore, there is a need for a prognostic study that identifies modifiable prognostic factors using a biopsychosocial view, that includes only patients with acute (0 to 3 weeks) or subacute (4 to 12 weeks) nonspecific idiopathic, non-traumatic neck pain, to help prevent chronification of pain in physiotherapy practices. This study should occur in primary care physiotherapy practices and with a cohort of patients of an adequate sample size.

The primary objective of this study is to identify which modifiable and non-modifiable factors are independent predictors of the development of chronic pain in patients with acute or subacute nonspecific idiopathic, non-traumatic neck pain, and secondly, to combine these to develop and internally validate a prognostic prediction model.

Methods

Study design

The present study is a prospective cohort study of prognostic factors informed by the PROGRESS framework and TRIPOD statement type 1b and specific recommendations for statistical approaches to Type 3 prognostic model research.^{27,28} This study will be reported in accordance with the Transparent Reporting of a multivariable prediction model for Individual Prognosis Or Diagnosis (TRIPOD) statement.²⁸

Study setting

Potential participants will be selected from 30 primary care physiotherapy practices including 81 physiotherapists between January 26, 2020, and August 31, 2022,

and is due to be completed at March 17, 2023 (including reminders and time for response).

For the generalizability of this research, we selected physiotherapists with different backgrounds; physiotherapists pursuing a master's degree working in primary care and experienced physiotherapists with and without affiliation to an academic institute will include participants.

Ethical approval

The Medical Research Ethics Committee approved that this study (protocol number: 19-766/C) does not apply to the Medical Research Involving Human Subjects Act (WMO). Therefore an official approval of this study by the Medical-Ethical Review Committee (METC) Utrecht is not required under the WMO Utrecht. All data is processed anonymously, and all participants have to sign an informed consent. The participants receive a personal code upon inclusion, which must be submitted at each measurement moment. The measurements will be collected through the secure data transfer system Formdesk.²⁹

Participants

The patients will be approached if they present with a new episode of acute (0 to 3 weeks) or subacute (4 to 12 weeks) nonspecific idiopathic, non-traumatic neck pain. To be eligible to take part in the study, participants must meet the following criteria:

1. The patients are at least 18 years or older.
2. The patients have a new presentation of neck pain not more than 12 weeks upon onset.
3. The neck pain region has to fall within the used region presented in Figure 4.1.
4. If the patient has had neck pain before, the patients must be relatively free from symptoms for at least three months (Numeric Pain Rating Scale (NPRS) of < 3) prior to this new episode of neck pain.

These inclusion criteria will effectively exclude the population with chronic pain.^{30,31}

The following general and specific exclusion criteria will be examined at an initial history taking by the physiotherapist prior to the recruitment:

Specific exclusion criteria:

1. Neck surgery in the past.
2. Cervical spine radiculopathy measured with the Upper Limb Neurodynamic Test 1.³³
3. Widespread pain (ICD 11); diffuse musculoskeletal pain in at least 4 of 5 body regions and in at least 3 or more body quadrant (as defined by upper-lower / left-right side of the body) and axial skeleton (neck, back, chest, and abdomen).
4. Pain not caused by a musculoskeletal origin (not located in the muscles, bones, joints, or tendons).³⁴

General exclusion criteria:

1. Inability to read or understand the Dutch language.

The participating physiotherapists record reasons for exclusion during the study period. In addition, an anonymized record will be kept of patients who meet the inclusion criteria but choose not to participate and their reasons for doing so. The treatment the patients receive will be reported. The coding will be done based on the Dutch Physiotherapy Guideline for neck pain.^{35,36} Participation in this study has no influence on the content of the treatment.

Baseline and follow-up procedure

If the patient meets the criteria during the first consultation, the physiotherapist informs the patient orally about the purpose and discusses participant expectations of the study. If the patient indicates verbally that he/she wants to participate in the study, written informed consent is obtained from the participant before the first questionnaire is completed. Subsequently, each participant receives a digital questionnaire sent via a link by email in week one (T0, baseline) and at six weeks (T1), three months (T2), and six months (T3). The T0 questionnaire takes 30–40 minutes to complete, the T1 measurement 20–30 minutes, and the T2 and T3 around 20 minutes. If the participant has not completed a questionnaire after one week, a reminder is sent by email or telephone contact will be made by the therapist who includes the participant. This procedure is repeated one week later, if necessary.

Outcome

The NPRS is used to quantify the presence of chronic pain. If pain is present at all measurement moments, six weeks, three months, and six months with a score of $\text{NPRS} \geq 3$, it will be classified as chronic pain.^{31,37} The NPRS is known to have an average reliability ($\text{ICC} = 0.67 [0.27-0.84]$) in neck pain, the minimal detectable change is 2.6 and a minimum clinically important difference of 1.5 in patients with mechanical neck pain.³⁸ The NPRS is an inventory and evaluation questionnaire, which was found to be valid.³⁹

Candidate prognostic factors

The candidate prognostic factors are based on our previous systematic review and Delphi study.^{16,25} From the systematic review, we included the variables significantly predictive of pain chronification or non-recovery. Furthermore, we included the variable with a consensus of $> 70\%$ in the first round of our Delphi study.

Table 4.1 shows the researched domains, candidate prognostic factors, the measure method used and how the variables will be handled in the statistical analysis.

Symptoms

The symptoms are current pain intensity (measured with the NPRS), duration of the neck pain in weeks, and whether the patient experiences pain in multiple body regions, all measured with a single question. Duration of pain will be handled as a continuous variable in our statistical analysis since there is no hard cut-off point between 'acute' and 'sub-acute' pain. Headaches are surveyed using a three-categorical single question to dichotomize specifically 'headaches that originated together with neck pain' and 'no headaches or headaches that exist before the neck pain'.

The Pain Disability Index (PDI) is a 7-item questionnaire that investigates the extent of self-reported pain-related disability.⁴⁰ The PDI measures family/home responsibilities, recreation, social activity, occupation, sexual behavior, self-care, and life support. The questionnaire items are assessed on a 0–10 numeric rating scale in which 0 means no disability and 10 is maximum disability.

Table 4.1: Candidate prognostic factors

Candidate prognostic factors	Measure	Range of the scale	Handling variables in statistical analysis
Patients' characteristics			
Sex	Self-report question	Male / Female	Dichotomous
Age	Self-report question	Age in years	Continuous
Symptoms			
Pain intensity at baseline	Numeric Pain Rating Scale (NPRS) "On a scale of 0 to 10, how much pain do you experience? Where 0 is no pain at all and 10 is the most imaginable pain"	0–10 Higher scores indicate a higher degree of pain.	Continuous
Duration of neck pain	In weeks	Number of weeks	Continuous
Reported pain in different body regions	Self-report question: Do you also experience pain in other parts of your body?	Yes / No	Dichotomous
Accompanying headache	Self-report question: Have you experienced accompanying headache(s) since you have neck pain?	Yes / No/ I had headache(s) before the neck pain.	Dichotomous 1 = Yes 2 = No or I had headaches before the neck pain
Disability	Pain Disability Index (PDI) is a 7-item questionnaire to investigate the magnitude of self-reported pain-related disability. (40) The PDI measures family/home responsibilities, recreation, social activity, occupation, sexual behavior, self-care, and life support(40)	0–70 Higher scores indicate higher interference of pain with daily activity.	Continuous The sum score will be divided by the entered items.

Work-related factors			
Happiness at work*	Self-report question: Can you indicate how happy you are with your current job?	Five point Likert scale. - Totally unhappy - Not happy - Neutral - Happy - Totally happy	Dichotomous 1 = Happy (happy and totally happy) 2 = Not happy (totally unhappy, not happy and neutral)
Job satisfaction*	Self-report question: How much satisfaction do you get from your current job?	Five point Likert scale. - Totally no satisfaction - No satisfaction - Neutral - Satisfaction - A lot of satisfaction	Dichotomous 1 = Satisfied (satisfaction and a lot of satisfaction) 2 = Not satisfied (totally no satisfaction, no satisfaction and neutral)
Potential to self-modify posture*	Self-report question: Are you able to change positions regularly during your work?	Five point Likert scale. - Completely impossible - Impossible - Neutral - Possible - Completely possible	Dichotomous 1 = Possible 2 = Impossible
General factors			
Lifestyle	Measured by the activity level according to the Dutch Healthy Exercise Norm	Dived into three categories: (1) I don't move 30 minutes any day a week of moderate intensity. (2) I'm exactly in between one and three (3) I am five days or more active per week	Dichotomous 1 = Achieving the Dutch Healthy Exercise Norm (category 3) 2 = Not achieving the Dutch Healthy Exercise Norm (category 1 and 2)
Physical activity			
Smoking	Self-report question: Do you smoke?	Yes / No	Dichotomous

Table 4.1 continues on next page.

Table 4.1: Continued

Candidate prognostic factors	Measure	Range of the scale	Handling variables in statistical analysis
Alcohol	Self-report question: Do you drink alcohol?	Yes / No	Dichotomous
Length and weight	Self-report question: What is your height? What is your weight?	Body Mass Index (BMI): weight/length x length in meters	Dichotomous
Sleep quality	Adjusted sleep quality question from the Neck Disability Index (NDI) and is subdivided in 4 domains; (1) wake up rested, (2) number of hours disturbed while sleeping, (3) fall asleep, and (4) personal experience sleep quality	(1) Yes / No (2) 0–5 Higher scores indicate more hours disturbed while sleeping (3) Yes / No difficulty falling asleep (4) Yes / No personal experience difficulty sleeping or falling asleep	Dichotomous 1 = No negative experience with sleeping (No negative score on one of the four domains) 2 = Negative experience with sleeping (a positive score on one of the four domains)
Psychological and behavior factors			
Catastrophizing	Pain Catastrophizing Scale (PCS) short version is a 6-item questionnaire that assesses catastrophic thoughts or feelings associated with the experience of pain(41)	0–24 Higher scores indicate more catastrophic thoughts	Continuous
Illness beliefs about recovery	Brief Illness Perception Questionnaire-Dutch language version (IPQ-DLV)(42) Two single questions: How long do you think your neck pain will continue? How concerned are you about your illness?	0–10 0 a very short time – 10 forever Higher scores indicate a maladaptive illness perception 0 not at all concerned – 10 extremely concerned Higher scores indicate a maladaptive illness perception	Continuous

Treatment beliefs	Brief Illness Perception Questionnaire-DLV(42) Single question: How much do you think your treatment can help your neck pain?	0–10 0 not at all – 10 extremely helpful A lower score indicates a maladaptive illness perception	Continuous
Depression	Depression Anxiety Stress Scale 21-item version (DASS-21)(43)	0–21 Higher scores indicate a higher degree of depression	Continuous
Kinesiophobia	Tampa Scale for Kinesiophobia (TSK) 11-item version(44)	11–44 Higher scores indicate a higher degree of kinesiophobia	Continuous
Distress	Depression Anxiety Stress Scale 21-item version (DASS-21)(43)	0–21 Higher scores indicate a higher degree of stress	Continuous
Coping	Pain Coping Inventory (PCI)(45) is a 33-items questionnaire and is subdivided into six scales: pain transformation, distraction, reducing demands, retreating, worrying, and resting Transforming the classification into an active (pain transformation, distraction and reducing demands) and passive coping strategy (retreating, worrying, resting)	Active coping = 12–48 Passive coping = 21–84	Dichotomous
Illness beliefs about pain identity	Brief Illness Perception Questionnaire-DLV(42) Single question: How well do you feel you understand your illness?	0–10 0 don't understand at all – 10 understand very clearly A lower score indicates a maladaptive illness perception	Continuous
Hypervigilance	Pain Vigilance Awareness Questionnaire (PVAQ)(46)	0–80 Higher scores indicate a higher degree of vigilance	Continuous
Self-efficacy	Pain Self-efficacy Questionnaire 2-item version(47)	0–12 Higher scores indicate a higher degree of self-efficacy	Continuous

Table 4.1 continues on next page.

Table 4.1: Continued

Candidate prognostic factors	Measure	Range of the scale	Handling variables in statistical analysis
Remaining factors			
Health care provider attitude*	Two vignettes consisting of 8 multiple choice questions and 4 open questions The open questions focused on the history taking, examination and treatment strategy The multiple-choice questions focus on the advice of the therapist with regard to categorizing of the complaint in type of seriousness, resumption of work and the implementation of daily activities	Biomedical Biopsychosocial	Dichotomous
Therapeutic relation*	Self-report question How much trust do you have in your healthcare provider/ physiotherapist?	0–10 0 no trust at all – 10 very much confidence	Continuous

* Candidate prognostic factors measured by an unvalidated measurement.

Work-related factors

The questions about happiness at work, job satisfaction, and the potential to self-modify posture during work are non-validated questions of which the psychometric properties are unknown and have been developed and formulated based on a Delphi study.²⁵ These are all answered on a Likert scale (1–5), which will be dichotomized in the statistical analysis (Table 4.1).

General factors

Lifestyle is measured with self-reported questions on different lifestyle domains; physical activity, smoking, alcohol, weight, and sleep quality.

Sleep quality is questioned through an adjusted question from the Neck Disability Index (NDI). The question was adjusted based on a Delphi study, which indicates that the NDI does not sufficiently question the ‘sleep quality’ factor.²⁵ For this reason, the statements “I do not wake up in the morning rested” and “I have trouble falling asleep” were added to the existing 9th question of the NDI questionnaire.⁴⁸ Since the question was modified, no psychometric properties are known.

Psychological and behavior factors

Catastrophizing is measured with a shortened validated 6-item version of the Pain Catastrophizing Scale (PCS) that assesses catastrophic thoughts or feelings associated with the experience of pain. Participants are asked to think about a recent painful experience and indicate to what extent they experience each of the six thoughts or feelings when they are in pain. The short version of the PCS assesses each dimension to capture the broad construct of catastrophizing; it comprises the lower-order factors labeled as rumination, magnification, and helplessness.⁴¹ It uses a 5-point scale ranging from 0 (not at all) to 4 (always).⁴⁹ A shortened version of the PCS is used to limit the total measurement duration. Internal, construct, and the smallest detectable change (SDC) are highly comparable to the original PCS.⁴¹

Kinesiophobia is measured using the Tampa Scale for Kinesiophobia 11-item version (TSK-11). This short version assesses both dimensions of kinesiophobia; harm and activity avoidance. The eleven questions are scored from 1 (strongly disagree) to 4 (strongly agree). The psychometric properties of the TSK-11 demonstrate good internal consistency ($\alpha = 0.79$), responsiveness (SRM = -1.11), test-retest reliability (ICC = 0.81, SEM = 2.54), concurrent validity and predictive validity.⁴⁴

In a (sub)acute state of pain, a response such as fear of movement or negative orientation toward pain could exist. However, it is not known when this response is a beneficial level of adaptation or an excessive response to (sub)acute pain. Furthermore, whether it is associated with developing chronicity in neck pain, a specific cut-off point to differentiate between these two levels does not exist. Therefore, our analyses will address catastrophizing and kinesiophobia as continuous factors.

The Depression Anxiety Stress Scale – 21 (DASS-21), recommended by Bijker et al.,⁵⁰ is used to map the degree of stress and depression. The DASS-21 consists of 21 questions with three subscales: depression, anxiety, and stress. Each subscale consists of 7 questions with the answer ranging from 0 (not applicable at all or never applicable) to 3 (very definitely or mostly applicable).⁴³ The internal consistency and test-retest reliability are sufficient for the DASS, and the convergent and divergent validity was supported.⁴³

The coping strategy of people with pain symptoms is measured through the Pain Coping Inventory List (PCI). This 33-item questionnaire reliably assesses six specific cognitive and behavioral strategies.^{45,51} The sensitivity and reproducibility of the PCI are acceptable.⁴⁵ Transforming the classification into an active or passive coping strategy is included in the content and construct validity. However, it has been validated in studies on chronic pain patients who experience physical complaints or (dis)function.⁵¹ The items are scored using an ordinal measurement level from 1 (rarely) to 4 (very common).

The illness perceptions are measured with the Illness Perception Questionnaire – Dutch language version (IPQ-DLV).⁴² The IPQ-K is a cross-culturally adapted Dutch version of the Brief Illness Perception Questionnaire (BIPQ).⁵² Four out of eight questions from the IPQ-DLV were included in this study to measure patients' illness perceptions about recovery, treatment beliefs, and pain identity. The IPQ-DLV is an easy-to-understand questionnaire for patients and healthcare professionals. Each question represents a different disease perception with a different outcome measure. The items are scored using an ordinal measurement level from 0–10. The questionnaire has moderate to substantial reliability, acceptable face validity, and acceptable content validity.⁴² The IPQ-K is an inventory questionnaire that can also be used evaluatively.⁴² The reproducibility appeared to be moderate to good.^{52–54}

The degree of vigilance is assessed by the 16-item Pain Vigilance Awareness Questionnaire (PVAQ). Respondents are asked to think about their behavior in

the past two weeks and indicate how often each item is a true reflection of their behavior or feelings. This questionnaire labeled two factors: “attention to pain” and “attention to changes in pain”. The degree of vigilance is rated on a 6-point scale ranging from 0 (never) to 5 (always).^{55,56} The PVAQ showed good validity, and internal consistency and fair test-retest reliability.^{46,55}

The short version of the Pain Self-Efficacy Questionnaire (PSEQ-2) is a robust measure of pain self-efficacy and is recommended by Sleijser-Koehorst et al.⁵⁷ It appears to be suitable for use in clinical and research settings.⁴⁷

Remaining modifiable factors

The therapist’s orientation, biomedical (BM) or biopsychosocial (BPS), is assessed by asking the therapist to fill in two vignettes. Vignettes are a realistic simulation of case situations in daily practice to measure of diagnosis or evaluation by health care providers. It is a promising quality rating for estimating the clinical behavior of care providers and, if constructed correctly, is a valid measuring instrument.^{58,59} Vignette 1 (acute non-specific neck pain) consists of open questions (4) and multiple-choice questions (4). The open questions focus on the history taking, examination, and treatment strategy. The multiple-choice questions focus on the therapist’s advice concerning the complaint in type and seriousness, resumption of work, and of daily activities. Vignette 2 (chronic non-specific neck pain) consist only of the multiple-choice questions (4). The vignettes used are based on standardized vignettes on low back pain.⁶⁰

In order to categorize the therapists (BM or BPS), the SCEBS method is used, covering Somatic, Psychological (Cognition, Emotion, and Behavior), and Social dimensions.⁶¹ A therapist with a biomedical orientation believes in a biomedical model of disease, where disability and pain are a consequence of a specific pathology within the spinal tissues, and treatment is aimed at treating the pathology and alleviating the pain.⁶⁰ A therapist with a biopsychosocial orientation believes in a biopsychosocial model of disease in which pain does not have to be a consequence of tissue damage and can be influenced by social and psychological factors.⁶⁰ The open questions are scored on the emergence of the different dimensions of the SCEBS, whereby the somatic dimension scores as a more biomedical orientation, and the dimensions cognition, emotion, behavior, and social score as biopsychosocial orientation. The multiple-choice questions score as a more biomedical orientation if the therapist is more likely to rate for spinal pathology, recommend

a delay in return to work and daily activity.^{62–64} The scores are merged at the end to a sum score, which categorize a therapist as BM or BPS. Every therapist is categorized by two researchers individually; after scoring, there will be a consensus meeting between the two researchers. A third reviewer makes the final decision if consensus cannot not be reached.

Therapeutic relation is measured by a self-developed single question of which psychometric properties are unknown and was formulated based on a Delphi study.²⁵

Sample size

To ensure the sample size is adequate in terms of the number of participants (n) and outcome events (E) relative to the number of predictor parameters (p) considered for inclusion, the minimum number of events per predictor parameter (EPP) is calculated recommended by Riley et al.⁶⁵ To reduce the risk of overfitting and to ensure that the overall risk is estimated precisely, the following criteria need to be met: (1) small optimism in predictor effect estimated as defined by a global shrinkage factor of ≥ 0.85 , (2) small absolute difference of ≤ 0.05 in the model's apparent and adjusted Nagelkerke's R^2 , and (3) precise estimation of the overall risk of rate in the population or similarly, precise estimation of the model intercept when predictors are mean-centered.⁶⁵ The calculation of the expected value of the (Cox-Snell) R-squared of the new model is based on two included prognostic models and is estimated at $R^2 = 0.23$.^{16,66,67} The outcome events (E) are estimated at 45% based on a systematic review by dividing the included number of patients by the number of non-recovery of pain.¹⁶ The number of included candidate predictor parameters for potential inclusion in the new model is based on a systematic review and a consensus study and is estimated at 26, of which 4 are non-modifiable and 22 are potentially modifiable. The a priori sample size calculation for the prognostic model suggests to include a minimum of 598 participants.

Statistical analysis methods and missing data

The statistical analysis is based on the 'Prognosis Research Strategy (PROGRESS) framework' type 3 research,²⁷ in which the step-by-step plan will be roughly as follows:

- Analysis of cases with and without the development of the outcome events (whether or not they developed chronic pain, respectively) will be done to determine if there are significant differences. In case $> 5\%$ of incomplete

records, data will be imputed. A multiple imputation strategy will be followed in case we assume data are at least missing at random. The number of imputations will be set to the percentage of incomplete records. Imputed values for continuous variables will be drawn using predictive mean matching. In case of evidence of data being MAR (or MCAR), the MAR assumption will be assessed by making a missingness indicator and testing whether incomplete patients differ from those that are incomplete.

- Identifying the independent predictive capacity of the candidate prognostic variables at baseline and the existence or non-existence of chronic pain measured at six weeks, three, and six months by univariable logistic regression analysis. These analyses will not be used to decide which prognostic factors will be included in the multivariable analyses.

If the sample size, as calculated, turns out to be adequate, all variables will be include in the multivariable analyses.

- Multicollinearity between candidate predictors will be assessed using the variance inflation factor. In case the variance inflation factor exceeds 10, we will select which candidate predictor add to the modeling phase based on clinical expertise.
- The non-variable factors of age, gender, and duration of the pain will be included to strengthen our model. The discriminative ability of the prognostic model will be determined based on the Area Under the receiver operating characteristic Curve (AUC), calibration will be assessed using a calibration plot and formally tested using the Hosmer and Lemeshow goodness-of-fit test, and model fit will be quantified as Nagelkerke's R^2 .
- Internal validation will be performed using bootstrap resampling to estimate the optimism-corrected AUC and to yield a measure of overfitting (i.e., the shrinkage factor). The shrinkage factor (a constant between 0 and 1) will be used to multiply the regression coefficient by. Generally, regression coefficients (and resulting predictions) are too extreme in case of overfitting, which is counteracted by the shrinking of regression coefficients.

Discussion

This prospective cohort study will be the most extensive study in this field to determines prognostic factors for the chronification of acute or subacute nonspecific idiopathic, non-traumatic neck pain in primary care physiotherapy. In contrast to most other prognostic research studies, this study has a biopsychosocial view

and focuses specifically on potentially modifiable factors by a physiotherapist. By selecting patients in primary care physiotherapy practices, we assume that they will represent the usual population consulting the physiotherapist with neck pain. The results of this study will improve the understanding of prognostic and potential protective factors, which will help clinicians guide their clinical decision making, develop an individualized treatment approach, and predict chronic neck pain more accurately.

The candidate prognostic factors in this study are mostly modifiable. The non-modifiable factors of increasing age, sex, duration of neck pain, and reported pain in different body regions have a known prognostic value for neck pain patients.^{10,15,23,68} Therefore these will be included in the model development to strengthen the value of our prognostic model. However, their non-modifiable nature means that they have limited use in potential prevention strategies. To pursue the clinical applicability of the model, other potentially relevant and modifiable factors are selected for inclusion based on our systematic review and international Delphi study.

Strengths and limitations

This study includes critical methodological features in order to minimize bias. These features include sampling a representative cohort from a physiotherapy setting with a high follow-up rate.⁶⁹ A new strategy for a representative sample size will be used. The rule-of-thumb events per variable (EPV) of ≥ 10 is widely used in the medical literature as the lower limit for developing prediction models that predict a binary outcome. However, this generally accepted minimal sample size criterion has been found lenient when default stepwise predictor selection strategies develop prognostic models. Earlier critiques on EPV as a sample size criterion have identified its weak theoretical and empirical underpinning.⁷⁰

The new strategy to achieve an accurate sample size offers us space for 26 candidate prognostic factors in model development to avoid overfitting in our analyses. Because more candidate prognostic factors can lead to model overfitting in small data sets, spurious observed relationships can occur because of regression value distortion and an overestimating predictive performance.^{65,71} The 26 candidate prognostic factors permitted are selected based on our previous systematic review and Delphi study to include only relevant and potential important factors.

Although this study does not influence the therapy the participants receive, the given therapy may influence the outcome and the accuracy and transportability

of the model to be developed.⁷² The patients receive standard care based on the Dutch Physiotherapy Guideline for neck pain.³⁵ They may include therapy to modify our candidate prognostic factors and thereby have a risk-reducing effect on chronicity. In addition, there may also be a form of ‘background treatment’; this could include any other treatment that an individual received during our prognostic study (e.g., psychological care) or changes an individual makes to their lifestyle.⁷² We will have no information on this form of treatment during this study; however, it could influence the outcome. Nevertheless, we consider the impact on our study findings to be minimal, given (1) the heterogeneity of the factors to be modified, (2) the multiple modalities used by physiotherapists, and (3) the difference in physiotherapists’ backgrounds. Thereby, we will report the physiotherapy treatment the patient received and discuss the possible impact on our study findings (TRIPOD 5C) but do not include the different treatments as a predictor in our model. Moreover, the current setting does reflect clinical practice as it is. This heterogeneity is likely to remain even after implementing of a well-performing model.

Clinical message and future directions

This study protocol describes only the first phase of prognostic model research; model development (including internal validation). Our model should be externally validated using data from another dataset to assess the generalizability of our prognostic model.⁷³ Thereafter, investigations of impact on decision-making and patient outcomes have to be done to measure our study’s clinical relevance and impact.

Acknowledgements

We want to thank all the physiotherapists who will include and follow their patients for six months. We would also wish to extend our special thanks to all the patients who will participate in this research.

We want to thank all reviewers, Assoc. Prof. Dr. Farnaza Ariffin, Prof. Alice Kongsted, and Ass. Prof. Yousef Alshere, for taking the time and effort necessary to review the manuscript. We sincerely appreciate all valuable comments and suggestions which helped us improve the manuscript’s quality.

References

1. Carroll LJ, Hogg-Johnson S, van der Velde G, Haldeman S, Holm LW, Carragee EJ, et al. Course and Prognostic Factors for Neck Pain in the General Population. *Eur Spine J*. 2008;17(S1):75–82.
2. Lee H, Hübscher M, Moseley GL, Kamper SJ, Traeger AC, Mansell G, et al. How does pain lead to disability? A systematic review and meta-analysis of mediation studies in people with back and neck pain. *Pain*. 2015;156(6):988–97.
3. GBD 2015 Disease and Injury Incidence and Prevalence Collaborators G 2015 D and II and P. Global, regional, and national incidence, prevalence, and years lived with disability for 310 diseases and injuries, 1990–2015: a systematic analysis for the Global Burden of Disease Study 2015. *Lancet (London, England)*. 2016;388(10053):1545–602.
4. Borghouts JAJ, Koes BW, Vondeling H, Bouter LM. Cost-of-illness of neck pain in The Netherlands in 1996. *Pain*. 1999;80(3):629–36.
5. Cohen SP. Epidemiology, diagnosis, and treatment of neck pain. *Mayo Clin Proc*. 2015;90(2):284–99.
6. Childs JD, Cleland JA, Elliott JM, Teyhen DS, Wainner RS, Whitman JM, et al. Neck Pain: Clinical practice guidelines linked to the international classification of functioning, disability, and health from the orthopedic section of the american physical therapy association. *J Orthop Sport Phys Ther*. 2008;38(9):A1–34.
7. Hurwitz EL, Randhawa K, Yu H, Côté P, Haldeman S. The Global Spine Care Initiative: a summary of the global burden of low back and neck pain studies. *Eur Spine J*. 2018;27(S6):796–801.
8. Veldkamp, R., Kruisselbrink, M., Meijer WM. Nivel Zorgregistraties Eerste lijn - Zorg door de fysiotherapeut; jaarcijfers 2020 en trendcijfers 2017-2020. NIVEL Zorgregistraties. Utrecht; 2022. 1–27.
9. Hush JM, Lin CC, Michaleff ZA, Verhagen A, Refshauge KM. Prognosis of Acute Idiopathic Neck Pain is Poor: A Systematic Review and Meta-Analysis. *YAPMR*. 2011;92: 824–9.
10. Wingbermühle RW, Chiarotto A, van Trijffel E, Koes B, Verhagen AP, Heymans MW. Development and internal validation of prognostic models for recovery in patients with non-specific neck pain presenting in primary care. *Physiother (United Kingdom)*. 2021;113:61–72.
11. Geneen LJ SB, Andrew Moore R, Clarke C, Martin D, Colvin LA, Smith BH. Physical activity and exercise for chronic pain in adults: an overview of Cochrane Reviews. *Cochrane Database Syst Rev*. 2017;4(4):CD011279.
12. Bertozzi L, Gardenghi I, Turoni F, Villafañe JH, Capra F, Guccione AA, et al. Effect of Therapeutic Exercise on Pain and Disability in the Management of Chronic Nonspecific Neck Pain: Systematic Review and Meta-Analysis of Randomized Trials. *Phys Ther*. 2013;93(8):1026–36.
13. Gross A, Langevin P, Burnie SJ, Bédard-Brochu M-S, Empey B, Dugas E, et al. Manipulation and mobilisation for neck pain contrasted against an inactive control or another active treatment. *Cochrane Database Syst Rev*. 2015;23(9).
14. Silva PV, Costa LOP, Maher CG, Kamper SJ, Costa LDCM. The new agenda for neck pain research: A modified delphi study. *J Orthop Sports Phys Ther*. 2019;49(9):666–74.

15. Wingbermühle RW, van Trijffel E, Nelissen PM, Koes B, Verhagen AP. Few promising multivariable prognostic models exist for recovery of people with non-specific neck pain in musculoskeletal primary care: a systematic review. *J Physiother*. 2018;64(1):16–23.
16. Verwoerd M, Wittink H, Maissan F, de Raaij E, Smeets RJEM. Prognostic factors for persistent pain after a first episode of nonspecific idiopathic, non-traumatic neck pain: A systematic review. *Musculoskelet Sci Pract*. 2019;42:13–37.
17. Walton DM. 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(1):494–505.
18. Kelly J, Ritchie C, Sterling M. Clinical prediction rules for prognosis and treatment prescription in neck pain: A systematic review. *Musculoskelet Sci Pract*. 2017;27:155–64.
19. Stenneberg MS, Rood M, de Bie R, Schmitt MA, Cattrysse E, Scholten-Peeters GG. To What Degree Does Active Cervical Range of Motion Differ Between Patients With Neck Pain, Patients With Whiplash, and Those Without Neck Pain? A Systematic Review and Meta-Analysis. *Arch Phys Med Rehabil*. 2017;98(7):1407–34.
20. Anstey R, Kongsted A, Kamper S, Hancock MJ. Are People With Whiplash-Associated Neck Pain Different From People With Nonspecific Neck Pain? *J Orthop Sport Phys Ther*. 2016;46(10):894–901.
21. Ris I, Juul-Kristensen B, Boyle E, Kongsted A, Manniche C, Søgaard K. Chronic neck pain patients with traumatic or non-traumatic onset: Differences in characteristics. A cross-sectional study. *Scand J Pain*. 2017;14:1–8.
22. Treede R-D, Rief W, Barke A, Aziz Q, Bennett MI, Benoliel R, et al. A classification of chronic pain for ICD-11. *Pain*. 2015;156(6):1003–7.
23. Verwoerd M, Wittink H, Maissan F, de Raaij E, Smeets RJEM. Prognostic factors for persistent pain after a first episode of nonspecific idiopathic, non-traumatic neck pain: A systematic review. *Musculoskelet Sci Pract*. 2019;42:13–37.
24. Riley RD, van der Windt DA, Croft P, Moons KG. *Prognosis research in healthcare Concepts, Methods, and Impact*. 1st ed. Oxford: Oxford University Press; 2019.
25. Verwoerd M, Wittink H, Maissan F, Smeets R. Consensus of potential modifiable prognostic factors for persistent pain after a first episode of nonspecific idiopathic, non-traumatic neck pain: results of nominal group and Delphi technique approach. *BMC Musculoskelet Disord*. 2020 Dec 7;21(1):656.
26. Turk DC, Okifuji A. Psychological Factors in Chronic Pain: Evolution and Revolution. *J Consult Clin Psychol*. 2002;70(3):678.
27. Steyerberg EW, Moons KGM, van der Windt DA, Hayden JA, Perel P, et al. Prognosis Research Strategy (PROGRESS) 3: Prognostic Model Research. *PLoS Med*. 2013;10(2).
28. Collins GS, Reitsma JB, Altman DG, Moons KGM. Transparent reporting of a multivariable prediction model for individual prognosis or diagnosis (TRIPOD): The TRIPOD statement. *BMJ*. 2015;350:1–9.
29. Innovero Software Solutions B.V. Formdesk. Available from: en.formdesk.com.
30. Van Tulder M, Becker A, Bekkering T, Breen A, Del Real MTG, Hutchinson A, et al. Chapter 3: European guidelines for the management of acute nonspecific low back pain in primary care. *Eur Spine J*. 2006;15(SUPPL. 2):169–91.
31. Traeger A, Henschke N, Hübscher M, Williams CM, Kamper SJ, Maher CG, et al. Development and validation of a screening tool to predict the risk of chronic low back pain in patients presenting with acute low back pain: A study protocol. *BMJ Open*. 2015;5(7).

32. 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):1648–54.
33. Thoomes EJ, van Geest S, van der Windt DA, Falla D, Verhagen AP, Koes BW, et al. Value of physical tests in diagnosing cervical radiculopathy: a systematic review. *Spine J*. 2018;18(1):179–89.
34. Hoy DG, Smith E, Cross M, et al. The global burden of musculoskeletal conditions for 2010: an overview of methods. *Ann Rheum Dis*. 2014;73:982–9.
35. BierI JD, Scholten-Peeters GGM, Staal JB, Pool J, van Tulder M, Beekman E, et al. KNGF Guideline Neck Pain. *R Dutch Soc Phys Ther*. 2016;5.
36. Bier JD, Scholten-Peeters GGM, Staal JB, Pool J, van Tulder M, Beekman E, Meerhoff GM, Knoop J, Verhagen AP. KNGF-richtlijn Nekpijn - praktijkrichtlijn. 2016.
37. Kamper SJ, Maher CG, Herbert RD, Hancock MJ, Hush JM, Smeets RJ. How little pain and disability do patients with low back pain have to experience to feel that they have recovered? *Eur Spine J*. 2010;19(9):1495–501.
38. Young IA, Dunning J, Butts R, Mourad F, Cleland JA. Reliability, construct validity, and responsiveness of the neck disability index and numeric pain rating scale in patients with mechanical neck pain without upper extremity symptoms. *Physiother Theory Pract*. 2019;35(12):1328–35.
39. Ferraz MB, Quaresma MR, Aquino,LR, Atra E, Tugwell P, Goldsmith C. Reliability of pain scales in the assessment of literate and illiterate patients with rheumatoid arthritis. *J Rheumatol*. 1990;17(8):1022–4.
40. Pollard CA. Preliminary validity study of the pain disability index. *Percept Mot Skills*. 1984;59(3):974.
41. McWilliams LA, Kowal J, Wilson KG. Development and evaluation of short forms of the Pain Catastrophizing Scale and the Pain Self-efficacy Questionnaire. *Eur J Pain (United Kingdom)*. 2015;19(9):1342–9.
42. de Raaij EJ, Schröder C, Maissan FJ, Pool JJ, Wittink H. Cross-cultural adaptation and measurement properties of the Brief Illness Perception Questionnaire-Dutch Language Version. *Man Ther*. 2012;17(4):330–5.
43. de Beurs E, Van Dyck R, Marquenie LA, Lange A, Blonk RWB, deBeurs E, et al. De DASS: een vragenlijst voor het meten van depressie, angst en stress. *Gedragstherapie*. 2001;34(1):35–54.
44. Woby SR, Roach NK, Urmston M, Watson PJ. Psychometric properties of the TSK-11: A shortened version of the Tampa Scale for Kinesiophobia. *Pain*. 2005;117(1–2):137–44.
45. Kraaimaat FW, Evers AWM. Pain-Coping Strategies in Chronic Pain Patients: Psychometric Characteristics of the Pain-Coping Inventory (PCI). *Int J Behav Med*. 2003;10(4):343–63.
46. Roelofs J, Peters ML, Muris P, Vlaeyen JWS. Dutch version of the Pain Vigilance and Awareness Questionnaire: Validity and reliability in a pain-free population. *Behav Res Ther*. 2002;40(9):1081–90.
47. Nicholas MK, McGuire BE, Asghari A. A 2-item short form of the pain self-efficacy questionnaire: Development and psychometric evaluation of PSEQ-2. *J Pain*. 2015;16(2):153–63.
48. Vernon H, Mior S. The Neck Disability Index: a study of reliability and validity. *J Manip Physiol Ther*. 1991;Sep(14(7)):409–15.

49. Sullivan MJL, Thorn B, Haythornthwaite JA, Keefe F, Martin M, Bradley LA, et al. Theoretical perspectives on the relation between catastrophizing and pain. *Clin J Pain.* 2001;17(1):52–64.
50. Bijker L, Sleijser-Koehorst MLS, Coppieters MW, Cuijpers P, Scholten-Peeters GGM. Preferred Self-Administered Questionnaires to Assess Depression, Anxiety and Somatization in People With Musculoskeletal Pain – A Modified Delphi Study. *J Pain.* 2020;21(3–4):409–17.
51. Brown GK, Nicassio PM. Development of a questionnaire for the assessment of active and passive coping strategies in chronic pain patients. *Pain.* 1987 Oct 1;31(1):53–64.
52. Moss-Morris R, Weinman J, Petrie K, Horne R, Cameron L, Buick D. The revised Illness Perception Questionnaire (IPQ-R). *Psychol Heal.* 2002;17(1):1–16.
53. Witteman C, Bolks L, Hutschemaekers G. Development of the illness perception questionnaire mental health. *J Ment Heal.* 2011;20(2):115–25.
54. de Raaij EJ, Ostelo RWJG, Maissan JF, Pool J, Westers P, Wittink H. Illness perceptions associated with patient burden with musculoskeletal pain in outpatient physical therapy practice, a cross-sectional study. *Musculoskelet Sci Pract.* 2020;45:102072.
55. Kunz M, Capito ES, Horn-Hofmann C, Baum C, Scheel J, Karmann AJ, et al. Psychometric Properties of the German Version of the Pain Vigilance and Awareness Questionnaire (PVAQ) in Pain-Free Samples and Samples with Acute and Chronic Pain. *Int J Behav Med.* 2017;24(2):260–71.
56. Roelofs J, Peters ML, McCracken L, Vlaeyen JWS. The pain vigilance and awareness questionnaire (PVAQ): Further psychometric evaluation in fibromyalgia and other chronic pain syndromes. *Pain.* 2003;101(3):299–306.
57. Sleijser-Koehorst MLS, Bijker L, Cuijpers P, Scholten-Peeters GGM, Coppieters MW. Preferred self-administered questionnaires to assess fear of movement, coping, self-efficacy, and catastrophizing in patients with musculoskeletal pain – A modified Delphi study. *Pain.* 2019;160(3):600–6.
58. Peabody JW, Luck J, Glassman P, Jain S, Hansen J, Spell M, et al. Measuring the quality of physician practice by using clinical vignettes: A prospective validation study. *Ann Intern Med.* 2004;141(10).
59. Rutten GMJ, Harting J, Rutten STJ, Bekkering GE, Kremers SPJ. Measuring physiotherapists' guideline adherence by means of clinical vignettes: a validation study. *J Eval Clin Pract.* 2006 Oct;12(5):491–500.
60. Bishop A, Foster NE, Thomas E, Hay EM. How does the self-reported clinical management of patients with low back pain relate to the attitudes and beliefs of health care practitioners? A survey of UK general practitioners and physiotherapists. *Pain.* 2008;135(1–2):187–95.
61. Oostendorp RAB, Elvers H, Mikołajewska E, Laekeman M, Van Trijffel E, Samwel H, et al. Manual physical therapists' use of biopsychosocial history taking in the management of patients with back or neck pain in clinical practice. *Sci World J.* 2015;2015.
62. Simmonds MJ, Derghazarian T, Vlaeyen JWS. Physiotherapists' knowledge, attitudes, and intolerance of uncertainty influence decision making in low back pain. *Clin J Pain.* 2012;28(6):467–74.
63. Derghazarian T, Simmonds MJ. Management of low back pain by physical therapists in Quebec: How are we doing? *Physiother Canada.* 2011;63(4):464–73.

64. Houben RMA, Gijssen A, Peterson J, De Jong PJ, Vlaeyen JWS. Do health care providers' attitudes towards back pain predict their treatment recommendations? Differential predictive validity of implicit and explicit attitude measures. *Pain*. 2005;114(3):491–8.
65. Riley RD, Snell KIE, Ensor J, Burke DL, Harrell FE, Moons KGM, et al. Minimum sample size for developing a multivariable prediction model: PART II - binary and time-to-event outcomes. *Stat Med*. 2019;38(7):1276–96.
66. Hoving JL, De Vet HCW, Twisk JWR, Devillé WLJM, Van Der Windt D, Koes BW, et al. Prognostic factors for neck pain in general practice. *Pain*. 2004;110:639–45.
67. Pool JJM, Ostelo RWJG, Knol D, Bouter LM, De Vet HCW. Are psychological factors prognostic indicators of outcome in patients with sub-acute neck pain? *Man Ther*. 2010;15:111–6.
68. 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 Sport Phys Ther*. 2013;43(2):31–43.
69. Altman DG. Systematic reviews of evaluations of prognostic variables. *BMJ Clin Res*. 2001;323(7306):224–8.
70. van Smeden M, Moons KGM, de Groot JAH, Collins GS, Altman DG, Eijkemans MJC, et al. Sample size for binary logistic prediction models: Beyond events per variable criteria. *Stat Methods Med Res*. 2019;28(8):2455–74.
71. Peduzzi P, Concato J, Kemper E, Holford TR, Feinstein AR. A Simulation Study of the Number of Events per Variable in Logistic Regression Analysis. *J Clin Epidemiol*. 1996; 49(12):1373–9.
72. Pajouheshnia R, Damen JAAG, Groenwold RHH, Moons KGM, Peelen LM. Treatment use in prognostic model research: a systematic review of cardiovascular prognostic studies. *Diagnostic Progn Res*. 2017;1(1):1–10.
73. Riley RD, Hayden JA, Steyerberg EW, Moons KGM, Abrams K, Kyzas PA, et al. Guidelines and Guidance Prognosis Research Strategy (PROGRESS) 2: Prognostic Factor Research. *PLOS Med*. 2013;10(2):e1001380.





Chapter 5

Development and internal validation of a multivariable prognostic model to predict chronic pain after a new episode of non-specific idiopathic, non-traumatic neck pain in physiotherapy primary care practice

M.J. Verwoerd, H. Wittink, F. Maissan, M. Teunis, S.M.J. van Kuijk, R.J.E.M. Smeets

Published BMJ Open, 2024, August

Objective: To develop and internally validate a prognostic model to predict chronic pain after a new episode of acute or subacute nonspecific idiopathic, non-traumatic neck pain in patients presenting to physiotherapy primary care, emphasizing modifiable biomedical, psychological, and social factors.

Design: A prospective cohort study with a 6-month follow-up between January 2020 and March 2023.

Setting: 30 physiotherapy primary care practices.

Participants: Patients with a new presentation of nonspecific idiopathic, non-traumatic neck pain, with a duration lasting no longer than 12 weeks from onset.

Baseline measures: Candidate prognostic variables collected from participants included age and sex, neck pain symptoms, work-related factors, general factors, psychological and behavioral factors, and the remaining factors: therapeutic relation and healthcare provider attitude.

Outcome measures: Pain intensity at 6 weeks, 3 months, and 6 months on a Numeric Pain Rating Scale (NPRS) after inclusion. A NPRS score of ≥ 3 at each time point was used to define chronic neck pain.

Results: Sixty-two (10%) of the 603 participants developed chronic neck pain. The prognostic factors in the final model were sex, pain intensity, reported pain in different body regions, headache since and before the neck pain, posture during work, employment status, illness beliefs about pain identity and recovery, treatment beliefs, distress, and self-efficacy. The model demonstrated an optimism-corrected Area Under the Curve (AUC) of 0.83 and a corrected R^2 of 0.24. Calibration was deemed acceptable to good, as indicated by the calibration curve. The Hosmer-Lemeshow test yielded a p-value of 0.7167, indicating a good model fit.

Conclusion: This model has the potential to obtain a valid prognosis for developing chronic pain after a new episode of acute and subacute nonspecific idiopathic, non-traumatic neck pain. It includes mostly potentially modifiable factors for physiotherapy practice. External validation of this model is recommended.

Key words: Neck pain, prognostic model, modifiable factors, chronic pain

Introduction

Neck pain is a widespread and disabling health condition significantly impacting public health.^{1–3} It is ranked third in terms of years lived with disability in non-fatal diseases, with high costs due to extended work absence and healthcare utilization.⁴ Chronic neck pain is particularly costly,⁵ and the prevalence has increased by 21% from 2005 to 2015, affecting approximately 358 million people worldwide.⁶ The estimated global number of neck pain cases is projected to be 269 million (219–322) by 2050, an increase of 32.5% (23.9–42.3) from 2020 to 2050.⁷

Physiotherapy is a common first-line treatment; however, its effectiveness in patients with chronic pain is often only moderate.^{8–10} Consequently, identifying prognostic factors to predict chronic pain is a top priority for neck pain research and for clinical care.¹¹ By identifying these prognostic factors, especially modifiable factors, physiotherapists can make more informed decisions, potentially target modifiable factors, and prevent the development of chronic idiopathic neck pain.

The existing literature on prognostic models shows a low performance in predicting chronic neck pain.¹² Moreover, the external validity of current prognostic models in terms of pain and recovery outcomes have not been proven in patients with acute and subacute neck pain.¹³ This may be attributed to the inclusion of heterogeneous groups of patients for the development of these prognostic models, characterized by varying pain duration (acute, subacute < 12 weeks and chronic > 3 months), clinical symptoms and prognosis. Furthermore, the varying definitions of the outcome, including persistent and/or recurrent pain groups, contribute to the low performance of these models. Additionally, much of the prognostic research has predominantly focused on non-modifiable factors, such as age, pain duration and sex, neglecting potentially modifiable factors.¹² Incorporating modifiable factors has the potential to better tailor interventions to individual patients, which could enhance the model's applicability and relevance in clinical practice.

It is known that biomedical, psychological, and social factors provide a comprehensive understanding of the neurophysiological changes involved in developing chronic pain.¹⁴ Consequently, there is a compelling need for a biopsychosocial approach that specifically focuses on modifiable prognostic factors to predict chronic pain after a new episode of nonspecific idiopathic, non-traumatic neck pain. This study aimed to (1) identify which modifiable factors are independent prognostic factors of the development of chronic neck pain in patients with acute

and subacute neck pain, and (2) to develop and internally validate a model to predict chronic pain.

Methods

The methods of this study have been extensively described in the study protocol.¹⁵ Briefly summarized, the methods were as follows:

Study design

The present study is a prospective longitudinal cohort study that focuses on modifiable prognostic factors and follows the guidelines of the PROGRESS framework and TRIPOD statement type 1b.^{16,17} This study adheres to the specific statistical recommendations for Type 3 prognostic model research.¹⁶ The findings are reported according to the TRIPOD statement to ensure transparent reporting of the multivariable prediction model for individual prognosis (see Appendix 5.1).¹⁷

Study setting

Participants were recruited from 30 Dutch physiotherapy primary care practices by 94 physiotherapists between January 26, 2020, and August 31, 2022. The study was completed in March 2023 (including reminders and time for response).

Ethical approval

The Medical Research Ethics Committee Utrecht declared that the Medical Research Involving Human Subjects Act (WMO) does not apply to this study (protocol number 19-766/C). Participants who gave informed consent were assigned a unique code to allow anonymous data collection, facilitated through the secure Formdesk data transfer system.¹⁸

Participants

Patients were approached if they presented in one of the participating physiotherapy practices with a new episode of acute or subacute nonspecific idiopathic, non-traumatic neck pain. Patients were included if they met the following criteria: age 18 years or older, a new presentation of neck pain no longer than 12 weeks after onset and the patient indicated on the body diagram that he/she experienced regional neck pain. If the patient had a previous episode of neck pain, the patient had to be relatively free

from symptoms on the Numerical Pain Rating Scale (NPRS of < 3) for at least three months prior to the present episode of neck pain. The exclusion criteria were: neck pain surgery in the past, cervical spine radiculopathy assessed with the Upper Limb Neurodynamic Test 1,¹⁹ widespread primary pain (ICD-11) (diffuse musculoskeletal pain in at least 4 of 5 body regions (e.g. shoulder or upper arm, wrist or hand, pelvis, or ankle or foot) and in at least three or more body quadrants (as defined by upper-lower / left-right side of the body) and axial skeleton (neck, back, chest and abdomen),²⁰ pain not caused by musculoskeletal origin (not located in the muscles, bones, joints, or tendons),²¹ and inability to read or understand the Dutch language.

Baseline and follow-up procedure

During the first consultation, the physiotherapist informed eligible patients about the study purpose and expectations. Patients who verbally indicated they wanted to participate in the study, signed an informed consent before completing the initial digital questionnaire at baseline (T0). Follow-up questionnaires were sent via email at six weeks (T1), three months (T2), and six months (T3), taking 20–40 minutes to complete. Participants were reminded to complete the questionnaires via email or telephone contact by their treating physiotherapist.

Outcome

The NPRS was used to quantify the presence of chronic pain. If pain was present, defined as an NPRS ≥ 3 , at all measurement moments (i.e. six weeks, three months, and six months), it was classified as chronic.^{15,22}

Candidate prognostic factors

We included candidate prognostic factors to predict chronic pain or non-recovery identified in a previous systematic review and by neck pain experts in a Delphi study with $> 70\%$ consensus in the first round.^{12,23} Details on candidate prognostic factors and their measurement are provided in our study protocol.¹²

- **Patient characteristics:** sex and age.
- **Symptoms:** pain intensity at baseline measured with the NPRS, duration of the acute or subacute neck pain in weeks, reported pain in different body regions (yes/no), accompanying headache (since the onset of neck pain and headache before the neck pain), and disability measured with the Pain Disability Index, where the sum score was divided by the entered items (PDI).²⁴

- **Work-related factors:** happiness at work, job satisfaction, and potential to self-modify posture measured with a self-reported question.
- **General factors:** the lifestyle factors: smoking, alcohol, length and weight (body mass index), sleep quality measured with an adjusted sleep quality question from the Neck Disability Index (NDI),^{23,25} and physical activity measured by meeting the activity level according to the Dutch Healthy Exercise Norm (Yes/No).²⁶
- **Psychological and behavioral factors:** Illness perceptions were assessed using the Dutch version of the Brief Illness Perception Questionnaire (IPQ-DLV).²⁷ Catastrophizing was measured with the short version of the Pain Catastrophizing Scale (PCS).²⁸ Depression and distress were assessed with the 21-item version of the Depression Anxiety Stress Scale (DASS-21).²⁹ Kinesiophobia was measured using the 11-item version of the Tampa Scale for Kinesiophobia (TSK).³⁰ Coping strategies were evaluated with the Pain Coping Inventory (PCI).^{31,32} Hypervigilance was assessed using the Pain Vigilance and Awareness Questionnaire (PVAQ),³³ and self-efficacy in managing pain was measured with the 2-item version of the Pain Self-Efficacy Questionnaire.³⁴
- The **remaining factors** included, first, the ‘therapeutic relationship’, assessed through the self-reported question: ‘How much trust do you have in your healthcare provider/physiotherapist?’. Second, the ‘therapist’s orientation’, which could be either biomedical or biopsychosocial. The authors categorized this orientation based on open-ended and multiple-choice questions about neck pain cases.¹⁵

Sample size

To ensure a sufficient sample size to reduce the effect of overfitting, the minimum number of events per candidate prognostic factor was calculated as recommended by Riley et al.³⁵ The expected value of the Cox-Snell R-squared of the new model was estimated at 0.23,^{23,36,37} and the estimated outcome event rate at 45%.¹² The study considered 26 candidate prognostic factors, including four non-modifiable and 22 potentially modifiable prognostic factors. The a priori sample size calculation suggested a minimum of 598 participants for the prognostic model.

Statistical analysis methods and missing data

This study followed the Prognosis Research Strategy (PROGRESS) framework type 3 research.¹⁶ The Statistical software IBM SPSS (version 27) and R (version 4.2.2) were used for the statistical analysis.^{38,39} For the analysis, we extensively utilized the following R packages: tidyverse, MASS, pROC and Mice.^{40–43} The complete R script used in this study can be found on GitHub at <https://github.com/uashogeschoolutrecht/painr> (see Appendix 5.2 the table of contents).

We used multiple imputation with fully conditional specification to impute incomplete records, assuming data to be at least missing at random (MAR).⁴⁴ Predictive mean matching was used to impute continuous variables, and logistic regression for categorical variables. After completing the data, the outcome variable (chronic pain) was determined for each participant. The factor ‘healthcare provider orientation’ exhibited significant missing data, which could not be imputed based on patient-specific information. As a result, we had to proceed with the available data during the subsequent analysis, even though a significant portion was missing.

The predictive performance of each candidate prognostic factor of chronic pain was estimated using univariable logistic regression analysis. These analyses were not used to decide which prognostic factors would be included in the multivariable model.

Before multivariable modeling, we computed the variance inflation factor (VIF) to assess multicollinearity. If this factor exceeded 10, the selection of candidate prognostic factors for modeling was guided by the clinical expertise of the authors of this study.

All candidate prognostic factors were entered into the multivariable model. To make the model more concise and to identify the most significant prognostic factors, we applied backward elimination.

Model performance was quantified as its discriminative ability, using the Area Under the receiver operating characteristic Curve (AUC), model calibration, using calibration plots and computing the Hosmer and Lemeshow goodness-of-fit test, and as model fit, using Nagelkerke’s R^2 .

Bootstrap resampling with 1000 bootstrap samples was utilized for internal validation to calculate the optimism-corrected AUC and determine the shrinkage factor, thereby adjusting for overfitting by shrinking regression coefficients. After shrinking regression coefficients, we re-estimated the model intercept.

Results

A total of 2,567 patients underwent eligibility assessment across 30 physiotherapy practices in the Netherlands. Among these patients, 1,600 were excluded, primarily due to the fact they already had chronic pain (lasting > 12 weeks with a NPRS $\geq$ 3), cervical spine radiculopathy, or widespread pain. Additionally, 307 patients refused to participate, citing disinterest, scheduling conflicts, or stress at the time of invitation. Ultimately, 660 potential participants provided informed consent, however, 58 of them did not respond during the baseline measurement phase, resulting in the inclusion of 603 individuals in a period of 2.5 years (Figure 5.1). Among them, 62 participants (10%) developed chronic pain, while 541 participants experienced recovery from their pain.

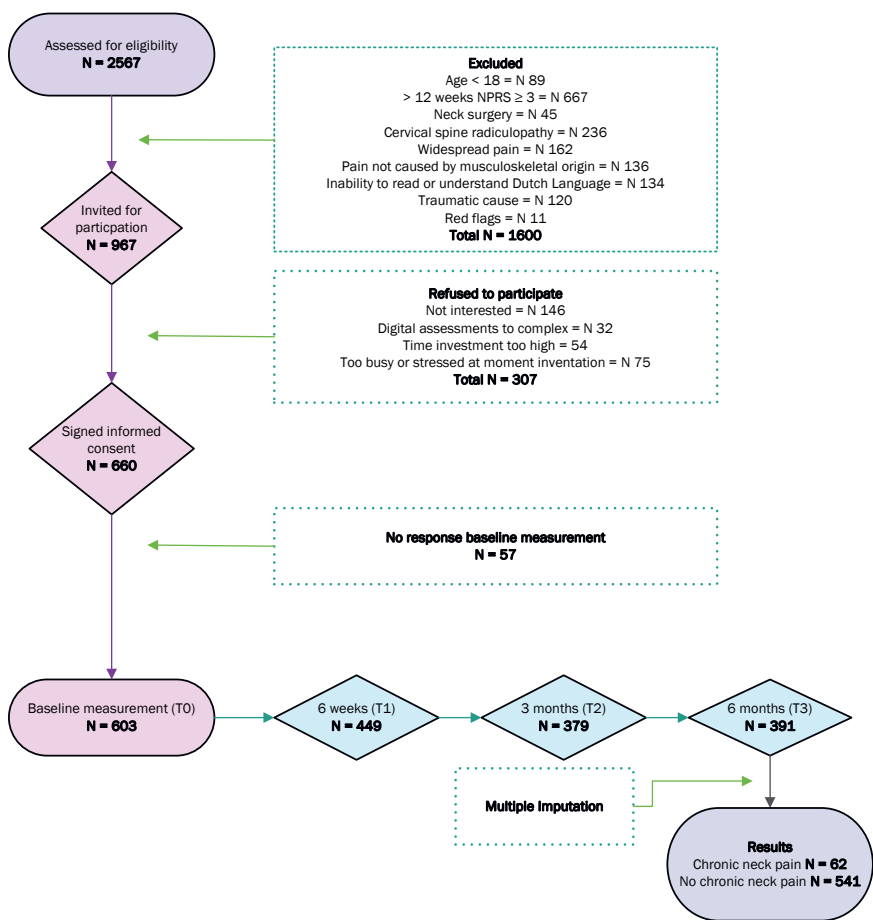


Figure 5.1: Flow-chart study.
N = Number, T = Time-point.

For the description of the participants' characteristics, including candidate prognostic factors, and the number of participants with missing data, see Table 5.1. We included 397 women and 206 men. The mean pain intensity at baseline was 5.9 (SD 1.9), and the mean disability was relatively low, with a score of 2.7 (SD 2.1) on a 0–7 scale. Of our 603 participants, 92 (15.3%) did not work. We included these participants as not working in all the work-related factors in our multivariable analyses.

Table 5.1: Baseline characteristics of the study population

	Number (percent)	Mean (SD) Median (IQR)	Missing count (percent)
Patients characteristics			
Sex			
1 = Male	206 (34.2)		0 (0)
2 = Female	397 (65.8)		
Age		44.5 (15.7) 44.0 (31–56)	1 (.2)
Symptoms			
Pain intensity at baseline (0–10)		5.9 (1.9)	0 (0)
Higher scores indicate a higher degree of pain		6 (5–7)	
Duration of neck pain		4.5 (2.9)	0 (0)
Number of weeks		4 (2–6)	
Recurrent pain			1 (.2)
1 = No	198 (32.8)		
2 = Yes	404 (67)		
Reported pain in different body regions			4 (.7)
1 = No	210 (34.8)		
2 = Yes	389 (64.5)		
Accompanying headache			5 (.8)
1 = No	247 (41)		
2 = Yes	281 (46.6)		
3 = I had headache(s) before the neck pain	70 (11.6)		
Disability (0–7)		2.73 (2.1)	1 (.2)
Higher scores indicate higher interference of pain with daily activity. The sum score divided by the entered items.		2.3 (1.0–4.1)	
Work-related factors			
Work status			10 (1.7)
1 = Yes	501 (83.1)		
2 = No	92 (15.3)		
Education			16 (2.7)
0 = Low level of education	313 (51.9)		
1 = High level of education	274 (45.4)		

Table 5.1 continues on next page.

Table 5.1: Continued

	Number (percent)	Mean (SD) Median (IQR)	Missing count (percent)
Happiness at work			23 (3.8)
1 = Happy (ref)	376 (62.4)		
2 = Neutral or not happy	112 (18.6)		
3 = Not working	92 (19)		
Job satisfaction			21 (3.5)
1 = Satisfied (ref)	404 (67)		
2 = Neutral or not satisfied	86 (14.3)		
3 = Not working	92 (18.7)		
Potential to self-modify posture			25 (4.2)
1 = Possible (ref)	372 (61.7)		
2 = Neutral or impossible	114 (18.9)		
3 = Not working	92 (19.4)		
General factors			
Physical activity			8 (1.3)
0 = Achieving the Dutch Healthy Exercise Norm	219 (36.3)		
1 = Not achieving the Dutch Healthy Exercise Norm	376 (62.3)		
Smoking			3 (.5)
1 = No	528 (87.6)		
2 = Yes	72 (11.9)		
Alcohol			5 (.8)
1 = No	129 (21.4)		
2 = Yes	469 (77.8)		
BMI		25.31 (4.3) 24.66 (22.5–27.7)	
Sleep quality			2 (.3)
0 = No negative experience with sleeping	130 (21.6)		
1 = Negative experience with sleeping	471 (78.1)		
Psychological and behavior factors			
Catastrophizing (0–24)		4.58 (4.6)	3 (.5)
<i>Higher scores indicate more catastrophic thoughts</i>		3 (1–7)	
Illness beliefs about recovery (Duration 0–10)		4.13 (2.7)	10 (1.7)
0 a very short time – 10 forever		3 (2–6)	
<i>Higher scores indicate a maladaptive illness perception</i>			
Illness beliefs about recovery (Concerned 0–10)		3.96 (2.6)	8 (1.3)
0 Not at all concerned – 10 extremely concerned		4 (2–6)	
<i>Higher scores indicate a maladaptive illness perception</i>			
Treatment beliefs (0–10)		7.82 (1.9)	12 (2.0)
0 not at all – 10 extremely helpful		8 (7–9)	
<i>A lower score indicates a maladaptive illness perception</i>			

Table 5.1 continues on next page.

Table 5.1: Continued

	Number (percent)	Mean (SD) Median (IQR)	Missing count (percent)
Depression (0–21) <i>Higher scores indicate a higher degree of depression</i>		2.47 (3.3) 1 (0–4)	3 (.5)
Kinesiophobia (11–44) <i>Higher scores indicate a higher degree of kinesiophobia</i>		16.5 (5.2) 15 (12–20)	3 (.5)
Distress (0–21) <i>Higher scores indicate a higher degree of stress</i>		4.4 (4.1) 3 (1–7)	3 (.5)
Coping			5 (.8)
0 = Passive coping	120 (19.9)		
1 = Active coping	478 (79.3)		
Illness beliefs about pain identity (0–10) 0 don't understand at all – 10 understand very clearly <i>A lower score indicates a maladaptive illness perception</i>		6.11 (2.3) 6 (5–8)	14 (2.3)
Hypervigilance (0–80) <i>Higher scores indicate a higher degree of vigilance</i>		31.0 (11.4) 31 (23 – 38)	3 (.5)
Self-efficacy (0–12) <i>Higher scores indicate a higher degree of self-efficacy</i>		10.31 (2.3) 11 (10–12)	2 (.3)
Remaining factors			
Therapeutic relation (0–10) 0 no trust at all – 10 very much confidence		8.79 (1.4) 9 (8–10)	10 (1.7)
Health care provider attitude			
1 = Biomedical	134 (22.2)		49 (8.1)*
2 = Biopsychosocial	420 (69.7)		

* We missed the attitude measurement for 14 of the 94 physiotherapists, including a total of 49 patients.

There was some loss to follow-up at various follow-up moments. However, only 78 participants did not complete any follow-up measurement. At the 6-weeks measurement, 154 participants failed to submit the required forms. This number changed to 224 at the 3-months follow-up, and to 211 at the 6-month mark. The Little's MCAR test yielded a p-value greater than 0.05, supporting the appropriateness of multiple imputations.⁴⁴

The interventions most frequently applied were (1) joint mobilization, manipulation, traction, and nerve mobilization techniques, with an application rate of 85.4%, and (2) information and advice, with an application rate of 86.7%. Exercise and massage were applied to 58.1% and 54.7% of the study population. For a detailed overview of the interventions applied across the study population, see Appendix 5.3.

Univariable prognostic factors of development of chronic pain

The univariable analyses (see Figure 5.2) revealed significant positive associations between the following candidate prognostic factors and chronic pain: being female, higher pain intensity at baseline, longer duration of neck pain, experiencing pain in different body regions, onset of headache since the neck pain began, higher disability scores, unemployment, higher scores on catastrophizing, illness beliefs about recovery (concerned and duration), depression, distress, and lower treatment beliefs. Some of these factors were identified with broad confidence intervals (CI). For most factors not showing significant associations, the odds ratios (ORs) were close to one, indicating lack of a clinically meaningful association.

Multivariable modeling

The inclusion of ‘work status’ as a category among the work-related prognostic factors resulted in multicollinearity within the following factors: happiness and satisfaction at work, and the ability to change posture during work. To mitigate this issue, we decided to include only the factor ‘ability to change posture at work’ in our final model. This decision was based on the distinct conceptual domain of this factor, which differs from the psychological construct already well-represented by the other included factors. The candidate prognostic factor ‘work status’ is thus also referred to the ability to change posture at work in the analysis. Following this adjustment, multicollinearity was no longer observed.

Several prognostic factors were identified from the multivariable logistic regression analysis. These included sex (female), higher pain intensity at baseline, reported pain in different body regions, headache since the onset of neck pain, headache(s) before the neck pain, an inability or neutral score on self-modify posture during work, not working, lower scores pain identity and treatment beliefs, higher scores in beliefs regarding recovery (duration and concerns), and higher scores on distress and self-efficacy. The ORs including 95% confidence intervals are presented and visualized in Figure 5.3. Of all prognostic factors, not working showed the strongest association (OR: 4.87). The combined prognostic model showed an Area Under the Curve (AUC) of 0.86 (95% Confidence Interval: 0.82 to 0.90) and a Nagelkerke’s R^2 of 0.31 (Figure 5.4). The Hosmer-Lemeshow test yielded a p-value of 0.7167, indicating good model fit. The calibration plot (Figure 5.4) revealed acceptable to good calibration over the range of predicted probabilities. The Brier score was 0.077, indicating solid performance.

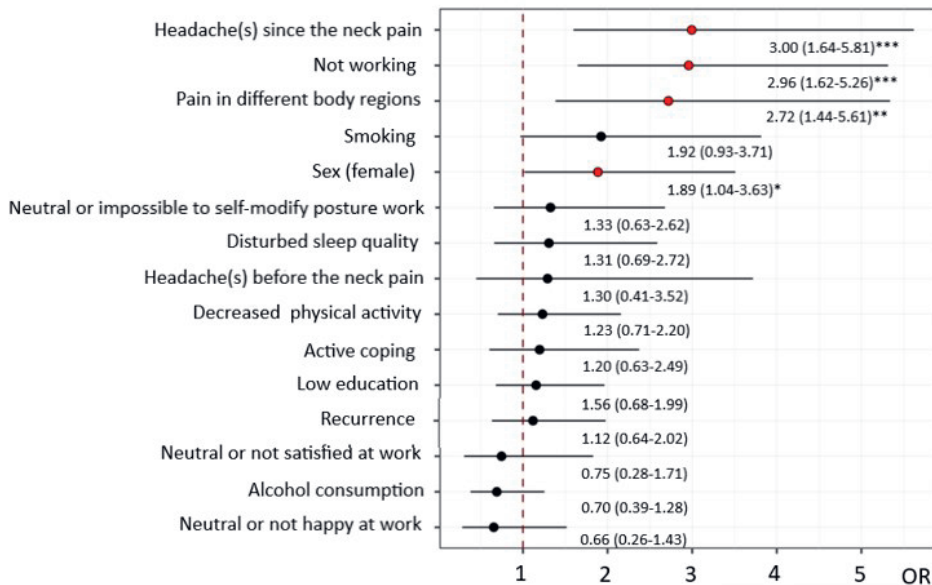
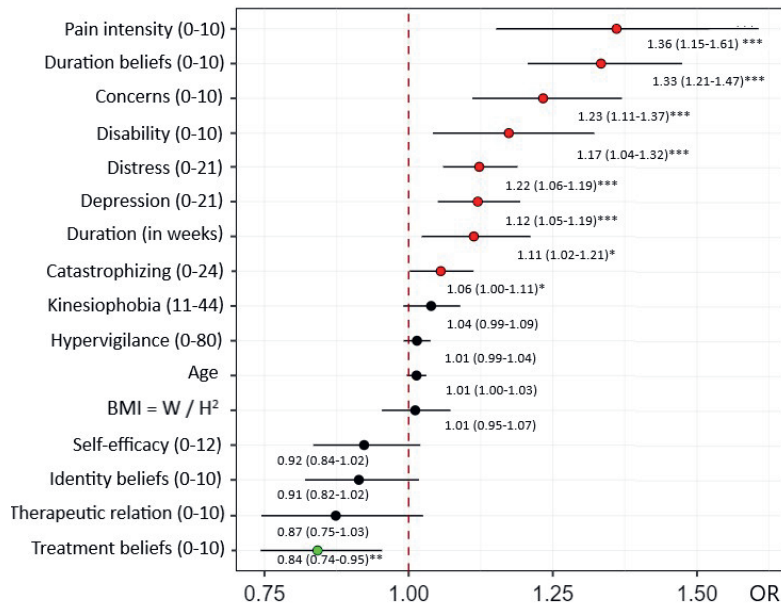


Figure 5.2: Univariable logistic regression analysis: unadjusted association between each candidate prognostic factor and the outcome of chronic pain.

The first figure displays the continuous variables, while the second illustrates the categorical and dichotomous variables and Odds Ratio (OR) and corresponding confidence intervals (CI) are presented. BMI denotes Body Mass Index, W represents Weight (kg), and H stands for Height (m). P-values are indicated as follows: * for $0.01 < p \leq 0.05$, ** for $0.001 < p \leq 0.01$, and *** for $p \leq 0.001$.

	Regression coefficient after shrinkage	Odds Ratio (95% Confidence Interval)	P-value
Intercept	-5.782		
Sex (female)	0.468	1.76 (0.90 - 3.61)	0.107
Pain intensity at baseline (0-10)	0.227	1.32 (1.08 - 1.62)	0.008 **
Reported pain in different body regions (no/yes)	0.734	2.43 (1.19 - 5.35)	0.020 *
No headache(s) (<i>reference</i>)			
Headache(s) since the neck pain	0.726	2.41 (1.21 - 5.03)	0.015 *
Headache(s) before the neck pain	-0.070	0.92 (0.27 - 2.77)	0.885
Potential to self-modify posture (<i>reference</i>)			
Neutral or impossible	0.384	1.59 (0.71 - 3.43)	0.247
Not working	1.311	4.87 (2.29 - 10.43)	<0.001 ***
Illness beliefs about recovery Duration (0-10)	0.184	1.25 (1.11 - 1.42)	<0.001 ***
Illness beliefs about recovery Concerned (0-10)	0.108	1.14 (0.99 - 1.32)	0.075
Treatment beliefs (0-10)	-0.204	0.78 (0.67 - 0.92)	0.003 **
Distress (0-21)	0.083	1.11 (1.03 - 1.19)	0.006 **
Illness beliefs about pain identity (0-10)	-0.142	0.84 (0.73 - 0.97)	0.016 *
Self-efficacy (0-12)	0.109	1.14 (0.99 - 1.34)	0.086

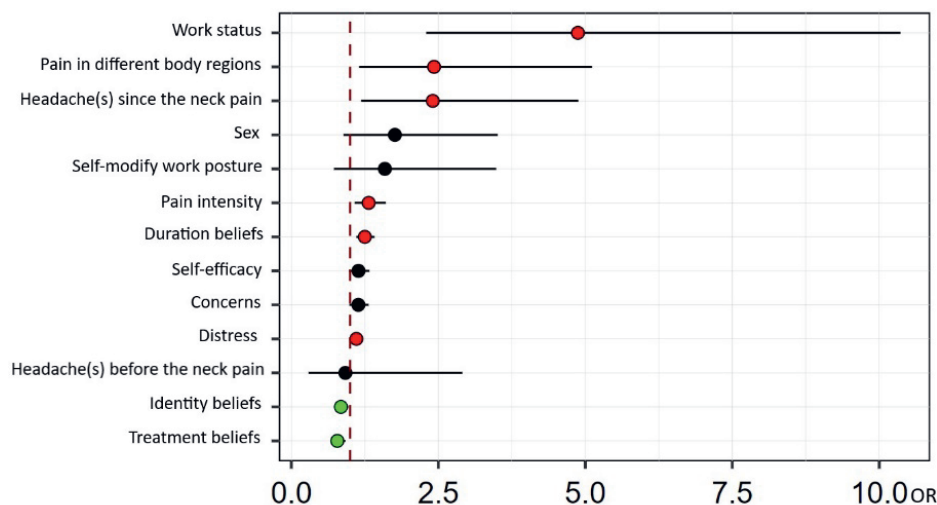


Figure 5.3: Adjusted multivariable logistic regression model.

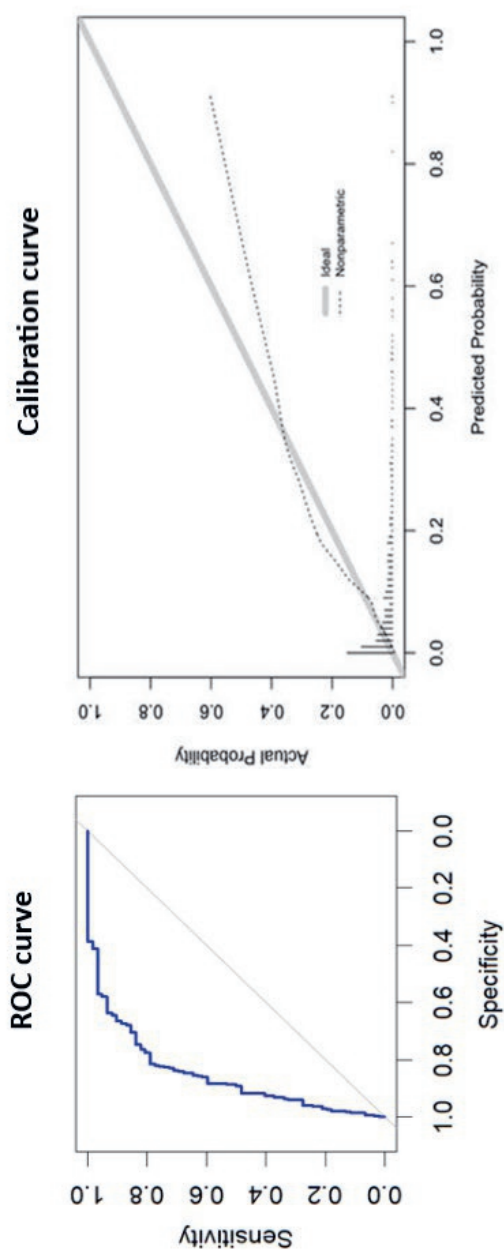


Figure 5.4: Area under the receiver operating characteristic and Calibration curve. The tick marks at the bottom of the Calibration curve represent the distribution of predicted probabilities. Each tick mark indicated a predicted probability for an individual observation. A dense cluster of tick marks indicated more observations with that specific predicted probability. This distribution occurs within the dataset.

Internal validation prognostic model

The bootstrap validation yielded a shrinkage factor of 0.83, which was then used to multiply the regression coefficients by. The resulting model, including re-estimated intercept are in Figure 5.3. The AUC after correction for optimism was 0.83. The optimism-corrected Nagelkerke's R^2 was 0.24.

The intermezzo section and Box 5.1 highlight a detailed a detailed patient profile to clarify the applicability and interpretation of our findings in a practical context. Supplemental Figure S5.1 presents an interactive visualization depicting the varied pain trajectories among participants within our cohort, alongside the linear predictor and the probabilities of chronic pain derived from our multivariable prognostic model. This visualization illustrates the complexity and variability of pain progression over time. For a comprehensive visualization of all participants, see the web application: <https://rstudio-connect.hu.nl/painr-app/>.

Intermezzo

The patient (participant 110), a male, describes his neck pain intensity as 6 on the Numeric Pain Rating Scale (NPRS) and reports also low back pain. Since the onset of neck pain, he has also developed headaches, which were not present before the neck pain. Despite being employed, he finds it impossible to modify his posture during work. He anticipates the duration of his symptoms to be quite long, assessing it at 9 out of 10. Despite this, his concern for his condition is relatively minimal, with a score of 2 out of 10. His confidence in the therapy is high, rated at 8 on a 0–10 scale. Stress is absent in his case, evidenced by a score of 0 out of 21. While he admits to only a moderate understanding of his pain, scoring a 6 out of 10, he shows a high level of self-efficacy, achieving a full score of 12 on a 0–12 scale.

The patient (participant 914), a female, reports experiencing a pain intensity level of 6 on the Numeric Pain Rating Scale (NPRS). She notes pain in other regions of her body as well. Since developing neck pain, she has also begun to experience headaches, which she did not have prior to the neck pain. Currently, she is not employed. She anticipates her symptoms will persist, rating the anticipated duration as 10 on a scale from 0 to 10, indicating a long-term expectation of symptoms. She expresses moderate concern about her neck pain, with a concern level of 5 on a 0–10 scale. Her confidence in the effectiveness of her therapy is also moderate, rated a 5 on a 0–10 scale. She reports experiencing a moderate level of stress,

scoring 12 on a 0–21 scale. Her self-reported understanding of her pain is 6 on a 0–10 scale, and scores a moderate self-efficacy, with a score of 6 on a 0–12 scale.

Box 5.1: Prognostic model application: Participant 110 en 914

Linear predictor (LP)

The linear predictor (LP) is given by:

$$\begin{aligned}
 LP = & -5.782 \\
 & + (0.468 \times \text{sex}[\text{female} = 1]) \\
 & + (0.227 \times \text{pain intensity}) \\
 & + (0.734 \times \text{pain in different body regions}) \\
 & + (0.726 \times \text{headache(s) since the neck pain}) \\
 & - (0.070 \times \text{headache(s) before the neck pain}) \\
 & + (0.384 \times \text{potential to self-modify posture at work}) \\
 & + (1.311 \times \text{work status}) \\
 & + (0.184 \times \text{duration beliefs}) \\
 & + (0.108 \times \text{concerns}) \\
 & - (0.204 \times \text{treatment beliefs}) \\
 & + (0.083 \times \text{distress}) \\
 & - (0.142 \times \text{identity beliefs}) \\
 & + (0.109 \times \text{self-efficacy})
 \end{aligned}$$

Probability of chronicity

Probability of chronicity

$$\text{Probability of chronicity} = \frac{1}{1 + e^{-LP}}$$

Participant 110

Linear predictor (LP) calculation for patient X yields $LP = -1.88$, resulting in:

$$\text{Probability of chronicity} = \frac{1}{1 + e^{1.88}} = 13.2\%$$

Participant 914

Linear predictor (LP) calculation for patient X yields $LP = 0.98$, resulting in:

$$\text{Probability of chronicity} = \frac{1}{1 + e^{-0.98}} = 72.7\%$$

Discussion

In this prospective cohort study, we (1) identified which (modifiable factors) are independent prognostic factors of the development of chronic neck pain, and we (2) developed and internally validated a prognostic model for predicting chronic pain after a new episode of acute or subacute nonspecific idiopathic, non-traumatic neck pain. We found several significant associations between non- and modifiable factors and chronic pain: being female, higher pain intensity at baseline, longer duration of neck pain, experiencing pain in different body regions, the onset of headache since the neck pain began, higher disability scores, unemployment, higher scores on catastrophizing, illness beliefs about recovery (concerned and duration), depression, distress, and lower treatment beliefs.

The internally validated prognostic model demonstrates good prognostic performance, underscored by an optimism-corrected AUC of 0.83. The calibration indicates a solid performance, as indicated by the calibration curve, alongside a commendable Brier score. The Hosmer-Lemeshow test, with a p-value of 0.717, affirms a good model fit. Nonetheless, the model's corrected R^2 of 0.24 suggests that the model provides a meaningful but limited explanation of the probability distribution of the outcome of chronic pain. The model comprises twelve variables, four non-modifiable and eight potentially modifiable by physiotherapists. The non-modifiable factors include sex, reported pain in different body regions, longer existing headaches, and employment status (not working). Potentially modifiable factors encompass baseline pain intensity, self-efficacy, headache onset concurrent with neck pain, the ability to self-modify posture at work, illness beliefs regarding recovery (including concerns and expected duration), and beliefs about neck pain identity and treatment.

When comparing our individual prognostic factors and those included in our prognostic model with existing prognostic studies in musculoskeletal pain, several common factors emerge, including age, work status, reported pain in different body regions (including headache), baseline pain identity, and self-efficacy.^{45–49} In our study, not working showed a high OR in both univariable and multivariable analyses. A physiotherapist cannot directly modify this factor; however, attention could be given to potentially modifiable factors associated with unemployment, such as physical disability and mental health.^{50,51} In addition, in our study, a higher score on the Pain Self-Efficacy Questionnaire 2-item version was associated with higher odds of chronic neck pain. Notably, this association was characterized by a

low regression coefficient and OR and was insignificant with a small CI. Moreover, this outcome may be biased using this short questionnaire, where the largest group of our population scored above 10 on a 0–12 point scale for self-efficacy, exhibiting a known ceiling effect.⁵² This notable outcome might, therefore, be questioned.

The illness perception factors: beliefs about recovery (including concerns and duration), identity, and treatment beliefs. Longitudinal studies on low back pain have yielded similar findings, illustrating individual associations between illness beliefs (e.g., duration and treatment beliefs) and negative clinical outcomes over various time periods.^{53–55} However, in prognostic multivariable models, the contribution of illness perceptions to the robustness of a prognostic model varies.^{55,56} Notably, illness beliefs are often excluded from the candidate prognostic factors in models developed and externally validated for neck pain models.^{12,57–59} Recent research has shown that modifying illness beliefs related to identity and concerns can mediate outcomes, specifically disability and pain, within physiotherapy primary care practices.⁶⁰ Consequently, further research into the modification of illness perception factors and their influence on the development of chronic pain, is imperative. Such studies are crucial to ascertain if physiotherapy interventions can effectively alter patients' outcomes.

Furthermore, it is important to note that several psychological factors, such as depression, kinesiophobia, catastrophizing, and poor coping skills, are commonly recognized as associated with and prognostic for chronic pain.^{14,61} These factors were not retained in our final prognostic model. Although these factors showed an association in our univariable analysis, they did not improve the predictive accuracy of our model. Notably, our baseline measurements indicated a distinctly non-normal distribution for these psychological factors, contrasting with studies in chronic pain patients where these factors are more prevalent.⁶¹ Despite their exclusion from our final model, screening for these factors during the initial pain phase and ongoing monitoring during recovery remain important. This is particularly noteworthy considering the body of evidence indicating that treatments targeting psychological factors, such as catastrophizing, depression, and distress, have shown favorable outcomes when addressed by healthcare providers. However, it is essential to highlight that these studies have primarily focused on patients with chronic musculoskeletal pain.^{62–66} In contrast, it is important to note that most studies involving patients with acute and subacute musculoskeletal pain have mainly focused on pain and disability as outcomes. However, these studies,

which investigate the effectiveness of treating physiological factors, should also examine whether identified changes in these psychological factors contribute to the reduction in pain intensity or disability observed in their study population.^{67–69}

The incidence of chronic pain in our participants differed from our systematic review findings. Our preliminary sample size calculation assumed a 45% chronicity rate for neck pain, which divided the number of patients by the non-recovery cases.¹² This disparity can be attributed to our definition of chronic pain and the definition of the measurement approach. Unlike most studies that use single time point assessment (e.g. 3, 6, or 12 months) with specific pain score threshold,⁷⁰ including those in our review,¹² our study used a more comprehensive approach. This approach provides a precise representation of chronic pain as a continuous experience. Using this methodology, we excluded the recurrent pain group, which includes pain-free or mild time periods, diverging from the International Classification of Diseases 11th Revision (ICD-11) broader definition of chronic pain.²⁰ We hypothesize that distinguishing between continuous and recurrent pain will lead to a more effective prognostic model, acknowledging the distinct pain experiences of these groups.

Limitations

The calibration curve suggests a substantial overestimation of higher risks; this estimation was based on only a few patients, as most had a relatively low estimated risk of chronic pain.

In the initial sample size calculation, we assumed a 45% incidence of chronic pain, based on our systematic review.¹² This calculation allowed for 26 candidate prognostic variables among a cohort of 598 participants.³⁵ However, this study yielded a lower-than-expected incidence of chronic pain, with only 10% of participants, indicating an underpowered and potentially inadequate sample size. However, the increased risk of overfitting and the potential for overly optimistic model performance seems to be minimal, as suggested by our internal validation analysis, which revealed a shrinkage factor close to one.

Chronic primary pain, as described by the ICD-11, is accompanied by significant emotional distress or functional disability. We used a threshold of ≥ 3 to define chronic pain based on the observation that mild pain typically does not entail marked emotional distress or functional disability.^{72,73} However, the literature indicates that establishing a definitive cut-off point for mild and moderate pain,

especially regarding pain-related interference with functioning and emotions, is complex.^{73–75} Therefore, choosing a threshold of 3 is debatable, and selecting a different threshold could yield different study results.

Furthermore, in our study's protocol discussion, we noted that our study did not influence the therapies participants received; however, these therapies could potentially affect both the outcomes and the accuracy and generalizability of the developed model. Participants were treated according to the Dutch Physiotherapy Guideline for neck pain, which might modify our candidate prognostic factors and potentially reduce chronicity risks. Given the diversity of factors, the variety of modalities used by physiotherapists, and the therapists' varied backgrounds, we considered the impact of these therapies on our study results minimal. Ideally, these therapies would either not be applied or should have been analyzed within the multivariable prognostic model to assess their impact; however, this was not feasible due to sample size constraints.

Our final prognostic model retained the factor 'self-modifying posture during work'. This factor was measured using a non-validated, subjective question, which may not accurately reflect the ability to change posture frequently. Patients often have difficulties accurately estimating their activity levels.^{71,72} Objective methods could provide more accurate information about participants' movement during work hours.

Clinical application and further research

The development of this prognostic model has identified several potential modifiable factors. In clinical practice, a physiotherapist can utilize this model to gain insight into a patient's probability of experiencing chronic neck pain. Furthermore, assessing and intervening on the modifiable factors in our model can be beneficial. However, we must be aware that although they have been validated for their prognostic value in our 1b prognostic study, it does not mean that modifying these factors will necessarily reduce the risk of developing chronicity. It is highly recommended to evaluate the performance of our model in an external validation study. If the model is found adequate, a prognostic model impact study is required, to quantify the effect on physiotherapist decision making in patients with acute or subacute nonspecific idiopathic, non-traumatic neck pain (TRIPOD statement).¹⁷

Conclusion

This model has the potential to obtain a valid prognosis for developing chronic pain after a new episode of acute or subacute nonspecific idiopathic, non-traumatic neck pain. It includes mostly potential modifiable factors for physiotherapy practice. External validation of this model is recommended.

Supplementary information

Acknowledgements

The authors would like to express their gratitude to all the physiotherapists who facilitated the inclusion of patients, and specifically to all the patients who participated in this study.

Contributors

All authors materially participated in this research. Their main contribution to the manuscript is described below:

Miss Martine Verwoerd: substantial contribution to study conception, study design, data analysis, data interpretation, drafting and revising the manuscript, and significant involvement in conceptualizing the web application and GitHub repository; dr. Harriet Wittink: substantial contribution to study conception, study design, data analysis, data interpretation, drafting and revising the manuscript; dr. Francois Maissan: contribution to study conception, study design, data interpretation and revising the manuscript; dr. Sander van Kuijk: substantial contribution to the study design, data analysis and data interpretation, drafting and revising the manuscript; dr. Marc Teunis: substantial contribution to the data analysis and data interpretation, revising the manuscript, and key architect of the web application and GitHub repository; Prof. dr. Rob J.E.M. Smeets: contribution to study conception, data analysis, data interpretation, drafting and revising the manuscript.

Data availability

Technical appendix, statistical code, and dataset available from the Github repository: <https://github.com/uashogeschoolutrecht/painr>. DOI: available upon acceptance.

Funding

This work was supported by the Institute of Movement Studies and partly by the Utrecht University of Applied Sciences research voucher. The funding concerns an internal promotion voucher of the University of Applied Sciences. The funders had no role in the study design, data collection, analysis, decision to publish, or manuscript preparation.

Competing interests

The authors have declared that no competing interests exist.

References

1. Carroll LJ, Hogg-Johnson S, van der Velde G, Haldeman S, Holm LW, Carragee EJ, et al. Course and Prognostic Factors for Neck Pain in the General Population. *European Spine Journal*. 2008;17(S1):75–82.
2. Hoy D, Geere JA, Davatchi F, Meggitt B, Barrero LH. A time for action: Opportunities for preventing the growing burden and disability from musculoskeletal conditions in low- and middle-income countries. *Best Pract Res Clin Rheumatol*. 2014;28(3):377–93.
3. Lee H, Hübscher M, Moseley GL, Kamper SJ, Traeger AC, Mansell G, et al. How does pain lead to disability? A systematic review and meta-analysis of mediation studies in people with back and neck pain. *Pain*. 2015;156:988–97.
4. GBD 2015 Disease and Injury Incidence and Prevalence Collaborators. Global, regional, and national incidence, prevalence, and years lived with disability for 310 diseases and injuries, 1990–2015: a systematic analysis for the Global Burden of Disease Study 2015. *Lancet*. 2016 Oct 8;388(10053):1545–602.
5. Childs JD, Cleland JA, Elliott JM, Teyhen DS, Wainner RS, Whitman JM, et al. Neck pain: Clinical practice guidelines linked to the international classification of functioning, disability, and health from the orthopaedic section of the american physical therapy association. *Journal of Orthopaedic and Sports Physical Therapy*. 2008;38(9).
6. Hurwitz EL, Randhawa K, Yu H, Côté P, Haldeman S. The Global Spine Care Initiative: a summary of the global burden of low back and neck pain studies. *European Spine Journal*. 2018;27(S6):796–801.
7. Valadan Tahbaz S, Elliott JM. Global, regional, and national burden of neck pain, 1990–2020, and projections to 2050: a systematic analysis of the Global Burden of Disease Study 2021. *Lancet Rheumatol*. 2024;6(3):e142–e155.
8. Geneen LJ SB, Andrew Moore R, Clarke C, Martin D, Colvin LA, Smith BH. Physical activity and exercise for chronic pain in adults: an overview of Cochrane. *Cochrane Database of Systematic Reviews*. 2017;4(4):CD011279.
9. Bertozzi L, Gardenghi I, Turoni F, Villafañe JH, Capra F, Guccione AA, et al. Effect of Therapeutic Exercise on Pain and Disability in the Management of Chronic Nonspecific Neck Pain: Systematic Review and Meta-Analysis of Randomized Trials. *Phys Ther*. 2013; 93(8):1026–36.
10. Gross A, Langevin P, Burnie SJ, Bédard-Brochu MS, Empey B, Dugas E, et al. Manipulation and mobilisation for neck pain contrasted against an inactive control or another active treatment. *Cochrane Database of Systematic Reviews*. 2015;23(9).
11. Silva PV, Costa LOP, Maher CG, Kamper SJ, Costa LDCM. The new agenda for neck pain research: A modified delphi study. *Journal of Orthopaedic and Sports Physical Therapy*. 2019;49(9):666–74.
12. Verwoerd M, Wittink H, Maissan F, de Raaij E, Smeets RJEM. Prognostic factors for persistent pain after a first episode of nonspecific idiopathic, non-traumatic neck pain: A systematic review. *Musculoskelet Sci Pract*. 2019;42:13–37.
13. Wingbermühle RW, Chiarotto A, van Trijffel E, Stenneberg MS, Kan R, Koes BW, et al. External validation and updating of prognostic models for predicting recovery of disability in people with (sub)acute neck pain was successful: broad external validation in a new prospective cohort. *J Physiother*. 2023 Apr;69(2):100–7.

14. Cohen SP, Vase L, Hooten WM. Chronic pain: an update on burden, best practices, and new advances. *Lancet*. 2021;397(10289):2082–97.
15. Verwoerd MJ, Wittink H, Maissan F, van Kuijk SMJ, Smeets RJEM. A study protocol for the validation of a prognostic model with an emphasis on modifiable factors to predict chronic pain after a new episode of acute- or subacute nonspecific idiopathic, non-traumatic neck pain presenting in primary care. *PLoS One*. 2023;18(1):e0280278.
16. Steyerberg, EW, Moons, KGM, van der Windt, DA, Hayden, JA, Perel, P et al. Prognosis Research Strategy (PROGRESS) 3: Prognostic Model Research. *PLoS Med*. 2013;10(2).
17. Collins GS, Reitsma JB, Altman DG, Moons KGM. Transparent reporting of a multivariable prediction model for individual prognosis or diagnosis (TRIPOD): The TRIPOD statement. *BMJ (Online)*. 2015;350:1–9
18. Innovero Software Solutions B.V. Formdesk. Available from: en.formdesk.com.
19. Thoomes EJ, van Geest S, van der Windt DA, Falla D, Verhagen AP, Koes BW, et al. Value of physical tests in diagnosing cervical radiculopathy: a systematic review. *Spine Journal*. 2018;18(1):179–89.
20. Treede RD, Rief W, Barke A, Aziz Q, Bennett MI, Benoliel R, et al. A classification of chronic pain for ICD-11. *Pain*. 2015;156(6):1003–7.
21. Hoy DG, Smith E, Cross M, et al. The global burden of musculoskeletal conditions for 2010: an overview of methods. *Ann Rheum Dis*. 2014;73:982–9.
22. Traeger A, Henschke N, Hübscher M, Williams CM, Kamper SJ, Maher CG, et al. Development and validation of a screening tool to predict the risk of chronic low back pain in patients presenting with acute low back pain: A study protocol. *BMJ Open*. 2015;5(7).
23. Verwoerd M, Wittink H, Maissan F, Smeets R. Consensus of potential modifiable prognostic factors for persistent pain after a first episode of nonspecific idiopathic, non-traumatic neck pain: results of nominal group and Delphi technique approach. *BMC Musculoskelet Disord*. 2020 Dec 7;21(1):656.
24. Pollard CA. Preliminary validity study of the pain disability index. *Percept Mot Skills*. 1984;59(3):974.
25. Vernon H, Mior S. The Neck Disability Index: a study of reliability and validity. *J Manipulative Physiol Ther*. 1991;Sep(14(7)):409–15.
26. National Youth Monitor of the Netherlands. Available from: <https://jeugdmonitor.cbs.nl/en/definitions/Dutch%20healthy%20exercise%20norm%3A%20NNGB%20%28Nederlandse%20Norm%20Gezond%20Bewegen%29>.
27. de Raaij EJ, Schröder C, Maissan FJ, Pool JJ, Wittink H. Cross-cultural adaptation and measurement properties of the Brief Illness Perception Questionnaire-Dutch Language Version. *Man Ther*. 2012;17(4):330–5.
28. McWilliams LA, Kowal J, Wilson KG. Development and evaluation of short forms of the Pain Catastrophizing Scale and the Pain Self-efficacy Questionnaire. *European Journal of Pain (United Kingdom)*. 2015;19(9):1342–9.
29. de Beurs E, Van Dyck R, Marquenie LA, Lange a, Blonk RWB, deBeurs E, et al. De DASS: een vragenlijst voor het meten van depressie, angst en stress. *Gedragstherapie*. 2001; 34(1):35–54.
30. Woby SR, Roach NK, Urmston M, Watson PJ. Psychometric properties of the TSK-11: A shortened version of the Tampa Scale for Kinesiophobia. *Pain*. 2005;117(1–2):137–44.

31. Kraaimaat FW, Evers AWM. Pain-Coping Strategies in Chronic Pain Patients: Psychometric Characteristics of the Pain-Coping Inventory (PCI). *Int J Behav Med*. 2003;10(4):343–63.
32. Brown GK, Nicassio PM. Development of a questionnaire for the assessment of active and passive coping strategies in chronic pain patients. *Pain*. 1987;31(1):53–64.
33. Roelofs J, Peters ML, McCracken L, Vlaeyen JWS. The pain vigilance and awareness questionnaire (PVAQ): Further psychometric evaluation in fibromyalgia and other chronic pain syndromes. *Pain*. 2003;101(3):299–306.
34. Nicholas MK, McGuire BE, Asghari A. A 2-item short form of the pain self-efficacy questionnaire: Development and psychometric evaluation of PSEQ-2. *Journal of Pain*. 2015;16(2):153–63.
35. Riley RD, Snell KIE, Ensor J, Burke DL, Harrell FE, Moons KGM, et al. Minimum sample size for developing a multivariable prediction model: PART II - binary and time-to-event outcomes. *Stat Med*. 2019;38(7):1276–96.
36. Hoving JL, De Vet HCW, Twisk JWR, Devillé WLJM, Van Der Windt D, Koes BW, et al. Prognostic factors for neck pain in general practice. *Pain*. 2004;110:639–45.
37. Pool JJM, Ostelo RWJG, Knol D, Bouter LM, De Vet HCW. Are psychological factors prognostic indicators of outcome in patients with sub-acute neck pain? *Man Ther*. 2010;15:111–6.
38. IBM Corp. IBM SPSS Statistics for Windows (Version 27.0) [computer software]. IBM Corp; 2020.
39. R Core Team. A Language and Environment for Statistical Computing. Vienna, Austria: R Foundation for Statistical Computing; 2018.
40. Venables WN, Ripley BD. *Modern Applied Statistics with S*. Fourth Edition. New York: Springer.
41. Wickham H, Averick M, Bryan J, Chang W, McGowan L, François R, et al. Welcome to the Tidyverse. *J Open Source Softw*. 2019;4(43):1686.
42. Buuren S van, Groothuis-Oudshoorn K. mice : Multivariate Imputation by Chained Equations in R. *J Stat Softw*. 2011;45(3).
43. Robin X, Turck N, Hainard A, Tiberti N, Lisacek F, Sanchez JC, et al. pROC: an open-source package for R and S+ to analyze and compare ROC curves. *BMC Bioinformatics*. 2011;12(1):77.
44. Pedersen A, Mikkelsen E, Cronin-Fenton D, Kristensen N, Pham TM, Pedersen L, et al. Missing data and multiple imputation in clinical epidemiological research. *Clin Epidemiol*. 2017;9:157–66.
45. Artus M, Campbell P, Mallen CD, Dunn KM, Van Der Windt DAW. Generic prognostic factors for musculoskeletal pain in primary care: a systematic review. *BMJ Open*. 2017;7.
46. Campbell L, Smith A, McGregor L, Sterling M. Psychological Factors and the Development of Chronic Whiplash Associated Disorder(s). *Clin J Pain*. 2018;34(8):1.
47. 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. *Journal of Orthopaedic & Sports Physical Therapy*. 2013;43(2):31–43.
48. Walton DM. 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(1):494–505.

49. Miles CL, Pincus T, Carnes D, Homer KE, Taylor SJC, Bremner SA, et al. Can we identify how programmes aimed at promoting self-management in musculoskeletal pain work and who benefits? A systematic review of sub-group analysis within RCTs. *Eur J Pain*. 2011 Sep;15(8):775.e1-11.
50. Leonardi M, Guido D, Quintas R, Silvaggi F, Guastafierro E, Martinuzzi A, et al. Factors Related to Unemployment in Europe. A Cross-Sectional Study from the COURAGE Survey in Finland, Poland and Spain. *Int J Environ Res Public Health*. 2018;15(4):722.
51. Giladi H, Scott W, Shir Y, Sullivan MJL. Rates and Correlates of Unemployment Across Four Common Chronic Pain Diagnostic Categories. *J Occup Rehabil*. 2015;25(3):648–57.
52. Foster NE, Bishop A, Thomas E, Main C, Horne R, Weinman J, et al. Illness perceptions of low back pain patients in primary care: What are they, do they change and are they associated with outcome? *Pain*. 2008;136(1):177–87.
53. Foster NE, Thomas E, Bishop A, Dunn KM, Main CJ. Distinctiveness of psychological obstacles to recovery in low back pain patients in primary care. *Pain*. 2010;148(3):398–406.
54. Fors M, Öberg B, Enthoven P, Schröder K, Abbott A. The association between patients' illness perceptions and longitudinal clinical outcome in patients with low back pain. *Pain Rep*. 2022;7(3):e1004.
55. de Raaij EJ, Wittink H, Maissan JF, Westers P, Ostelo RWJG. Limited predictive value of illness perceptions for short-term poor recovery in musculoskeletal pain. A multi-center longitudinal study. *BMC Musculoskelet Disord*. 2021;22(1):522.
56. Wingbermühle RW, Chiarotto A, van Trijffel E, Koes B, Verhagen AP, Heymans MW. Development and internal validation of prognostic models for recovery in patients with non-specific neck pain presenting in primary care. *Physiotherapy (United Kingdom)*. 2021;113:61–72.
57. Wingbermühle RW, van Trijffel E, Nelissen PM, Koes B, Verhagen AP. Few promising multivariable prognostic models exist for recovery of people with non-specific neck pain in musculoskeletal primary care: a systematic review. *J Physiother*. 2018;64(1):16–23.
58. Wingbermühle RW, Heymans MW, van Trijffel E, Chiarotto A, Koes B, Verhagen AP. External validation of prognostic models for recovery in patients with neck pain. *Braz J Phys Ther*. 2021;25(6):775–84.
59. de Raaij EJ, Wittink H, Maissan JF, Twisk J, Ostelo RWJG. Illness perceptions; exploring mediators and/or moderators in disabling persistent low back pain. Multiple baseline single-case experimental design. *BMC Musculoskelet Disord*. 2022;23(1):140.
60. Mills SEE, Nicolson KP, Smith BH. Chronic pain: a review of its epidemiology and associated factors in population-based studies. *Br J Anaesth*. 2019;123(2):e273–83.
61. Kamper SJ, Apeldoorn AT, Chiarotto A, Smeets RJEM, Ostelo RWJG, Guzman J, et al. Multidisciplinary biopsychosocial rehabilitation for chronic low back pain. Vol. 2014, *Cochrane Database of Systematic Reviews*. John Wiley and Sons Ltd; 2014.
62. Lyng KD, Djurtoft C, Bruun MK, Christensen MN, Lauritsen RE, Larsen JB, et al. What is known and what is still unknown within chronic musculoskeletal pain? A systematic evidence and gap map. *Pain*. 2023;164(7):1406–15.
63. De Baets L, Matheve T, Meeus M, Struyf F, Timmermans A. The influence of cognitions, emotions and behavioral factors on treatment outcomes in musculoskeletal shoulder pain: a systematic review. *Clin Rehabil*. 2019;33(6):980–91.

64. Milesl CL, Pincusl T, Carnesl D, Homerl KE, Taylorl SJC, Bremnerl SA, et al. Review: Can we identify how programmes aimed at promoting self-management in musculoskeletal pain work and who benefits? A systematic review of sub-group analysis within RCTs. *European Journal of Pain*. 2011;15(8).
65. Cuenca-Martínez F, López-Bueno L, Suso-Martí L, Varangot-Reille C, Calatayud J, Herranz-Gómez A, et al. Implementation of Online Behavior Modification Techniques in the Management of Chronic Musculoskeletal Pain: A Systematic Review and Meta-Analysis. *J Clin Med*. 2022;11(7).
66. Monticone M, Cedraschi C, Ambrosini E, Rocca B, Fiorentini R, Restelli M, et al. Cognitive-behavioural treatment for subacute and chronic neck pain. Vol. 2015, *Cochrane Database of Systematic Reviews*. John Wiley and Sons Ltd; 2015.
67. Marin TJ, Van Eerd D, Irvin E, Couban R, Koes BW, Malmivaara A, et al. Multidisciplinary biopsychosocial rehabilitation for subacute low back pain. Vol. 2017, *Cochrane Database of Systematic Reviews*. John Wiley and Sons Ltd; 2017.
68. Nicholas MK, Linton SJ, Watson PJ, Main CJ. Early Identification and Management of Psychological Risk Factors ('Yellow Flags') in Patients With Low Back Pain: A Reappraisal. 2011. Available from: <https://academic.oup.com/ptj/article/91/5/737/2735759>.
69. Struyf F, Geraets J, Noten S, Meeus M, Nijs J. A Multivariable Prediction Model for the Chronification of Non-traumatic Shoulder Pain: A Systematic Review. *Pain Physician*. 2016;19(2):1–10.
70. van Weering M, Vollenbroek-Hutten M, Hermens H. The relationship between objectively and subjectively measured activity levels in people with chronic low back pain. *Clin Rehabil*. 2011;25(3):256–63.
71. Vergauwen K, Huijnen IPJ, Smeets RJE, Kos D, van Eupen I, Nijs J, et al. An exploratory study of discrepancies between objective and subjective measurement of the physical activity level in female patients with chronic fatigue syndrome. *J Psychosom Res*. 2021; 144:110417.

Appendix 5.1: TRIPOD Checklist Prediction Model Development and Validation

Section/topic	Item	Checklist item	Page
Title and abstract			
Title	1	Identify the study as developing and/or validating a multivariable prediction model, the target population, and the outcome to be predicted.	1
Abstract	2	Provide a summary of objectives, study design, setting, participants, sample size, predictors, outcome, statistical analysis, results, and conclusions.	2
Introduction			
Background and objectives	3a	Explain the medical context (including whether diagnostic or prognostic) and rationale for developing or validating the multivariable prediction model, including references to existing models.	5-6
	3b	Specify the objectives, including whether the study describes the development or validation of the model or both.	5-6
Methods			
Source of data	4a	Describe the study design or source of data (e.g., randomized trial, cohort, or registry data), separately for the development and validation data sets, if applicable.	7
	4b	Specify the key study dates, including start of accrual; end of accrual; and, if applicable, end of follow-up.	7
Participants	5a	Specify key elements of the study setting (e.g., primary care, secondary care, general population) including number and location of centres.	7-8
	5b	Describe eligibility criteria for participants.	7-8
	5c	Give details of treatments received, if relevant.	Not applicable
Outcome	6a	Clearly define the outcome that is predicted by the prediction model, including how and when assessed.	8
	6b	Report any actions to blind assessment of the outcome to be predicted.	7-8
Predictors	7a	Clearly define all predictors used in developing or validating the multivariable prediction model, including how and when they were measured.	8-10
	7b	Report any actions to blind assessment of predictors for the outcome and other predictors.	7-8
Sample size	8	Explain how the study size was arrived at.	10
Missing data	9	Describe how missing data were handled (e.g., complete-case analysis, single imputation, multiple imputation) with details of any imputation method.	10-11
Statistical analysis methods	10a	Describe how predictors were handled in the analyses.	10-11
	10b	Specify type of model, all model-building procedures (including any predictor selection), and method for internal validation.	10-11
	10d	Specify all measures used to assess model performance and, if relevant, to compare multiple models.	10-11

Appendix 5.1 continues on next page.

Appendix 5.1: Continued

Section/topic	Item	Checklist item	Page
Risk groups	11	Provide details on how risk groups were created, if done.	Not applicable
Results			
Participants	13a	Describe the flow of participants through the study, including the number of participants with and without the outcome and, if applicable, a summary of the follow-up time. A diagram may be helpful.	12-16
	13b	Describe the characteristics of the participants (basic demographics, clinical features, available predictors), including the number of participants with missing data for predictors and outcome.	12-16
Model development	14a	Specify the number of participants and outcome events in each analysis.	13
	14b	If done, report the unadjusted association between each candidate predictor and outcome.	17-18
Model specification	15a	Present the full prediction model to allow predictions for individuals (i.e., all regression coefficients, and model intercept or baseline survival at a given time point).	17-20
	15b	Explain how to use the prediction model.	23-24
Model performance	16	Report performance measures (with CIs) for the prediction model.	19-22
Discussion			
Limitations	18	Discuss any limitations of the study (such as nonrepresentative sample, few events per predictor, missing data).	28
Interpretation	19b	Give an overall interpretation of the results, considering objectives, limitations, and results from similar studies, and other relevant evidence.	25-28
Implications	20	Discuss the potential clinical use of the model and implications for future research.	28-29
Other information			
Supplementary information	21	Provide information about the availability of supplementary resources, such as study protocol, Web calculator, and data sets.	30
Funding	22	Give the source of funding and the role of the funders for the present study.	30

Appendix 5.2: Table of contents**Link Github:**

<https://github.com/uashogeschoolutrecht/painr>

Table of Contents Published with Bookdown:

0. Introduction

1.1 Data Flow

1. Exploratory data analysis – Raw data

1.1 Suggested improvements of the code

1.2 Packages

1.3 Load data

1.4 First glimpse at missingness

1.5 Select relevant variables

1.6 Exploratory Data Analysis

1.7 Write table with all labels

1.8 Deal with 'work' variables

1.9 Recode physical_activity

1.10 Write subsetted data to disk

2. Imputation of missing values

2.1 Packages

2.2 Data

2.3 Prepare dataset for imputing

2.4 Convert all categorical vars to factors

2.5 Panel with all distributions

2.6 Imputation of missing values

2.7 Checking Missing Completely at Random (MCAR)

2.8 Missingness pattern

2.9 Define predictors to include in the imputations

2.10 Using the MICE package for imputation of missing values

2.11 Create predictorMatrix for MICE

2.12 Calculate percentage missing data and cases

2.13 Running the imputations

2.14 Inspect the imputations

2.15 Check convergence

2.16 Check for plausible values of imputation

2.17 Checking the used predictor matrix

2.18 Look at the datasets

2.19 Skimming the data

2.20 Add attitude

2.21 Save to disk

3. Statistical exploration

3.1 Packages

3.2 Data

3.3 Global parameters

3.4 Statistical analysis methods and missing data

3.5 Reformat dataframe to stacked format

3.6 Create time variable

3.7 Recode time

3.8 Adding baseline as time=0

3.9 Carry forward

3.10 Rework the graph above to get cumulative pain intensity scores

3.11 Get individual lines for each patient

- 3.12 Write to disk as excel file and Rds R binary file
- 3.13 Distribution of the data
- 3.14 Table: baseline characteristics of the included patients
- 3.15 Testing assumptions before backward analysis

4. Prognostic model

- 4.1 Packages
- 4.2 Data load
- 4.3 Clean data and rename vars
- 4.4 Exploratory data analysis
- 4.5 Variable analysis – independent predictive capacity
- 4.6 Relevel dichotomous variables
- 4.7 Multivariable logistic regression analysis
- 4.8 AUC
- 4.9 Calibration curve
- 4.10 Result cCalibration plot
- 4.11 Hoslem and Lemeshow
- 4.12 Model fit
- 4.13 Internal validation
- 4.14 Plot corrected AUC
- 4.15 Results
- 4.16 Correcting the variables coefficients
- 4.17 Calibration in the Large

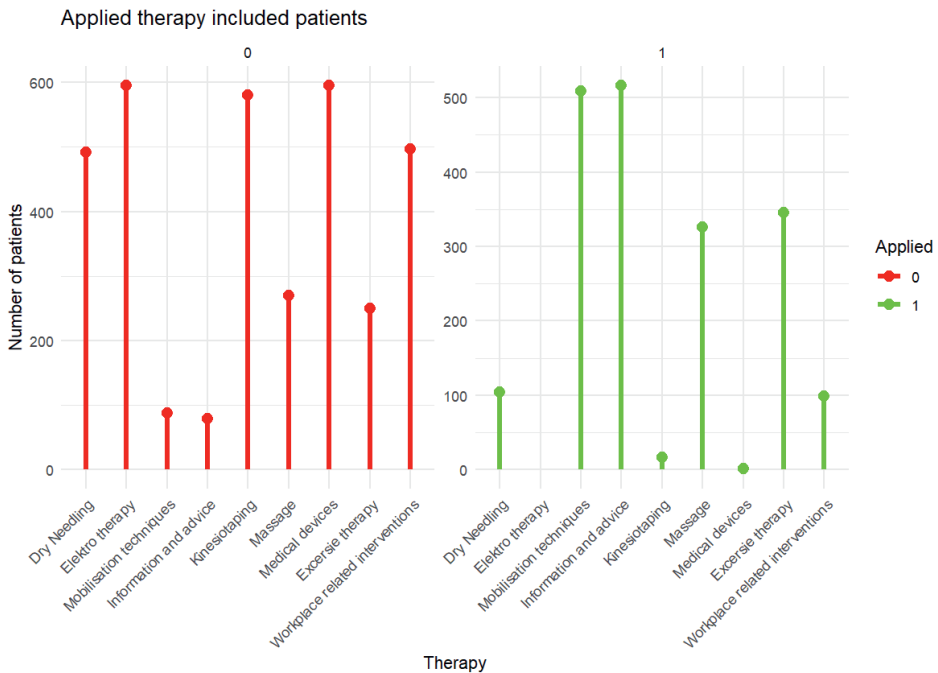
5. Article figures

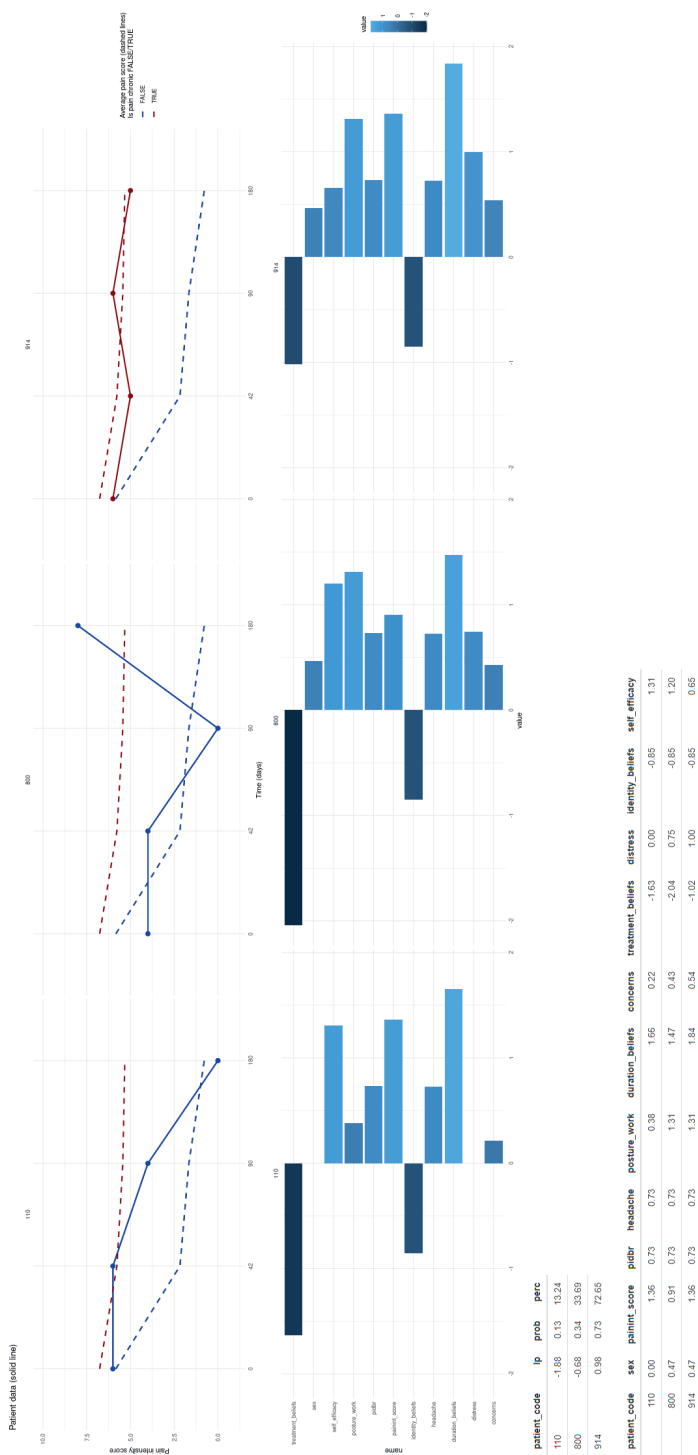
- 5.1 Packages
- 5.2 Data load
- 5.3 Clean data and rename variables
- 5.4 Exploratory data analysis
- 5.5 Variable analysis
- 5.6 Graph of model metrics
- 5.7 Relevel dichotomous variables
- 5.8 Refactor code above to a more compact version
- 5.9 Univariate analysis on the categorical variables
- 5.10 Visualize model outcome
- 5.11 Panel plot univariate
- 5.12 Multivariable logistic regression analysis
- 5.13 Backward model
- 5.14 Visualize backward model
- 5.15 Panel plot with all models
- 5.16 Rework figure labels
- 5.17 Figures for paper
- 5.18 Adding level info to figure
- 5.19 GGpubr panel
- 5.20 Area under the receiver operating characteristic Curve (AUC)
- 5.21 Calibration curve
- 5.22 Formally testing the Goodness-of-fit using the Hosmer and Lemeshow
- 5.23 Intermezzo – linear predictors

Appendix 5.3: Overview applied interventions study population

Table and Figure: Intervention included patients (N = 596)

Interventions	Number of patients	Applied (%)	Number of patients	Not applied (%)
1. Workplace, ergonomic and working time advice	99	16.6	497	83.4
2. Medical devices, collar or cervical pillow	1	0.2	595	98.2
3. Joint mobilizations, manipulation, traction, nerve mobilization techniques	509	85.4	86	14.6
4. Exercise therapy	346	58.1	250	41.9
5. Electrotherapy, laser, ultrasound, shockwave or heat therapy	0	0	596	100
6. Dry needling	492	17.4	104	82.6
7. Information and advice	79	86.7	517	13.3
8. Kinesiotaping	16	2.7	580	97.3
9. Massage	326	54.7	270	45.3

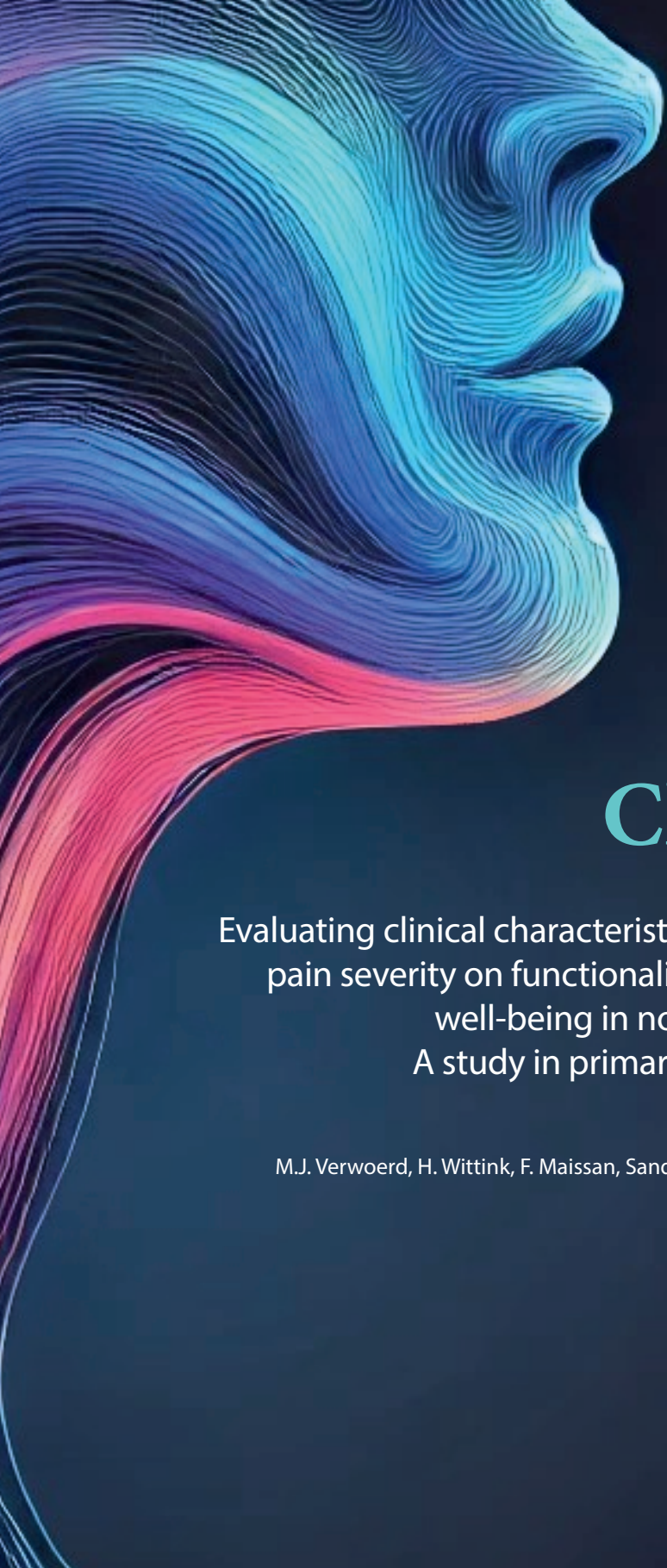




Supplemental Figure S5.1: Interactive visualization of patients' pain trajectories and chronicity probability.

For the visualization of all participants, see: <https://rstudio-connect.hu.nl/painr-app/>. In this visualization, "FALSE" indicates no chronic pain (pain < 3 at 6 weeks, 3 months, and 6 months), while "TRUE" denotes chronic pain (pain ≥ 3 at all time-points: 6 weeks, 3 months, and 6 months). The X-axis represents the pain score, measured using the Numerical Pain Rating Scale (0–10), and the Y-axis shows the cumulative number of days after the baseline measurement. "Patient_code" is a unique identifier for each patient. "Ip" stands for linear predictor, "Prob" represents the probability of chronicity, and "Perc" indicates the percent probability of chronicity. The bar graph and various values per variable illustrate the regression coefficient, multiplied by the patient data at baseline, across different variables from the prognostic model.





Chapter 6

Evaluating clinical characteristics and the impact of
pain severity on functionality and psychological
well-being in non-specific neck pain:
A study in primary physiotherapy care

M.J. Verwoerd, H. Wittink, F. Maissan, Sander M.J. van Kuijk, R.J.E.M. Smeets

Under review

Objective: (1) This study compares clinical characteristics between patients experiencing their first episode of nonspecific neck pain (NSNP) and patients with a new episode of NSNP in a recurrent pattern. Additionally, (2) it aims to investigate the difference in daily activities and psychological well-being between patients with mild pain (1–2 Numeric Pain Rating Scale (NPRS)) and moderate to severe pain (≥ 3 NPRS) at six weeks after their first presentation in practice.

Setting: 30 primary physiotherapy practices.

Participants: Patients with a new presentation of NSNP, lasting no longer than 12 weeks from onset.

Methods: Longitudinal observational cohort study with cross-sectional analysis.

Measurements: For hypothesis 1, participants' neck pain symptoms, prior conditions, work-related factors, general factors, psychological factors, and behavioral factors at baseline and pain intensity at six-week, three-month, and six-month follow-ups were collected. For hypothesis 2, participants' pain intensity, psychological factors and disability were measured.

Results: No clinically meaningful differences were found in clinical characteristics or recovery rates at six weeks, three months, and six months between patients experiencing a first episode of NSNP and those with recurrent episodes in primary physiotherapy care. However, significant differences were noted in how mild (1–2 NPRS) or moderate to severe pain (≥ 3 NPRS) interfered with disability, patient concerns, and self-efficacy at six weeks. Patients with higher pain intensity scored higher on disability, lower on the self-efficacy questionnaire and reported a higher level of concerns. These differences are considered clinically meaningful in disability, with a 1.33-point difference (SD 0.84–1.81) on a 0–7 scale, in self-efficacy, with a -1.25-point difference (SD -1.84 to -0.65) on a 0–12 self-efficacy scale, and patient concerns of 1.87-point difference (SD 1.21–2.52) on a 0–10 scale.

Conclusion: There are no clinically meaningful differences in clinical characteristics or pain recovery rates between a first-episode pain period and a new episode of acute pain in a recurrent patron in NSNP. Significant and clinically meaningful differences exist in the impact of pain severity on daily activities, patient concerns, and self-efficacy.

Key words: Neck pain, pain severity, recurrence, classification

Introduction

Effective classification of patients with nonspecific neck pain (NSNP) is important for optimizing intervention strategies, improving prognostic accuracy in clinical decision-making, and facilitating clinical research by studying homogeneous patient groups.¹ Existing treatment-based classification systems are diverse² and often lack accuracy.^{3–5} In the ICD-11, the International Association for the Study of Pain (IASP) categorizes chronic pain into secondary pain, which is related directly to a disease, and primary pain, which is considered a disease in its own right.⁶ Chronic primary musculoskeletal pain (CPP) is defined as pain persisting or recurring over three months, causing significant emotional distress or functional disability without direct attribution to a known disease.⁷

The ICD-11 highlights the need for a multimodal approach that integrates psychological, social, and biological factors in assessing and treating chronic pain.^{6,7} It also recommends optional specifiers for pain intensity, pain-related interference with daily functioning, and pain-related distress aligned with WHO severity stages.⁸ These are measured using a numeric rating scale (NRS) and subsequently translated into severity stages: ‘mild’ (≤ 3 NRS), ‘moderate’ (4–6 NRS), and ‘severe’ (≥ 7 NRS) to enhance clinical communication and research interpretability.⁹ However, significant variability in diagnostic and prognostic studies regarding the chronification of pain raises questions about whether the new definition of chronic pain, combined with the optional multidimensional rating system, effectively addresses this variability and, thereby, the effectiveness of this new definition of chronic pain.

Moreover, while the definition of CPP excludes acute pain, it encompasses recurrent pain, which may present as acute episodes, often exhibiting mild symptoms that minimally impact emotional well-being and functionality.^{6,7,9–12} These findings challenge the current classification of the ICD-11, highlighting the need to reevaluate whether (1) recurrent pain must be a part of the definition and (2) whether the pain severity stage should be mandatory instead of optional in defining CPP.

Given these considerations, our study aims to explore the distinctions in clinical presentations among NSNP patient groups and examine the impact of pain intensity on daily functioning and psychological well-being. We use the classification from our previous prognostic study to classify patients based on their first and new episodes in a recurrent pattern, as well as their pain intensity scores, to classify a patient as chronic or non-chronic.¹³ Therefore, we hypothesized that:

1. There is no clinically meaningful difference between the clinical presentations (e.g. lifestyle, psychological, behavior factors) or the six-week, three-month, and six-month recovery rates of patients experiencing their first episode of NSNP and those with a new episode in a recurrent pattern who present themselves in primary physiotherapy practice at baseline.
2. There is a clinically meaningful difference between groups with differing levels of pain severity (NPRS 1–2 defined mild pain, and NPRS ≥ 3 defined moderate and severe pain) on daily activities, illness perceptions, and psychological factors measured at 6 weeks follow-up.

Method

Study design

For this study, we used data from a larger prospective cohort study to identify prognostic factors for patients experiencing (sub)acute neck pain in primary physiotherapy practices in the Netherlands.¹³ This study encompasses a cross-sectional analysis of patient presentations at baseline and the six-week follow-up time-point and a longitudinal observation of patient outcomes over six weeks, three months, and six months. For hypothesis 1 we used baseline data (cross-sectional) and the pain measurements at six weeks, three months, and six months (longitudinal). For hypothesis 2, we used data obtained six weeks after their first presentation in primary physiotherapy practices (cross-sectional). We used the STROBE statement for cross-sectional and cohort studies as a reporting guideline.¹⁴

Ethical approval

Ethical Approval for this study was obtained from the Medical-Ethical Review Committee (METC) of the University Medical Center Utrecht (protocol number: 19-766/C). In adherence to privacy standards, all data were processed anonymously, with each participant providing informed consent. Data were securely collected and transmitted using Formdesk, a secure data management system.¹⁵

Setting

Potential participants were selected from 30 private physiotherapy practices that employed 94 physiotherapists. The participants' recruitment extended between

January 26, 2020, and August 31, 2022, and the follow-up was completed on March 17, 2023.

Participants

Eligibility for participation was extended to patients presenting with a new episode of (sub)acute nonspecific idiopathic, non-traumatic neck pain. Inclusion criteria were being 18 years or older, having a new onset of neck pain not exceeding twelve weeks, and having neck pain shaded in the area defining regional neck pain, located from the linea nuchae superior to the scapular spine (see Appendix 6.1). Patients with a history of neck pain were required to have been relatively symptom-free for a minimum of three months (NPRS of < 3) before the current episode. Exclusion criteria were previous neck surgery, cervical spine radiculopathy as determined by the Upper Limb Neurodynamic Test 1,¹⁶ widespread pain as defined in the ICD-11 (diffuse musculoskeletal pain in a minimum of four out of five body regions and at least three body quadrants), pain not caused by musculoskeletal origin, and an inability to read or understand the Dutch language.

For hypothesis 2, we used the same participants six weeks after their first presentation at the physiotherapist; however, we used only data of the patients who still experienced neck pain. At this time point, we categorized patients into the mild pain (1–2 NPRS) and moderate to severe pain groups (≥ 3).

Variables and measurements

At baseline, we assessed variables to differentiate between first-time and recurrent (sub)acute NSNP patients and the outcome variable pain intensity at six weeks, three months and six months (Hypothesis 1). At the six-week follow-up measurement, we assessed disability status, patient perceptions, psychological variables and sleep quality to analyze differences in these variables between the mild and moderate-severe pain groups (Hypotheses 2). All variables and their measurement moment are outlined in Figure 6.1, and their measurement method in Appendix 6.2.

Study size

Our sample size calculation revealed that to have 90% power for an independent-sample T-test to detect a medium effect size (quantified as Cohen's d of 0.5), we would need about 121 patients per group, when testing with an alpha of 0.05. Consequently, the smallest group must at least include 121 patients, assuming a

1:1 ratio. For analyses involving dichotomous and categorical variables, where 1 to 3 degrees of freedom are considered for various variables and adopting Cohen’s convention of a medium effect size ($w = 0.3$), we estimated a required sample size ranging from 165 to 230 participants. The power analysis for the regression analysis, predicting a small effect size (f^2), with a power of 80% and a significance level of 0.05, and considering the maximum number of variables in the model, indicates a minimum requirement of 108 participants in total.

Hypothesis 1 There is no clinically meaningful difference between the clinical presentation or the six-week, three-month, and six-month recovery rates of patients experiencing their first episode of NSNP and those with a new episode in a recurrent pattern who present themselves in primary physiotherapy practice.	
Baseline	Symptoms: Pain intensity at baseline, Duration of Neck Pain, Reported Pain in different body regions, Accompanying headache, Disability Lifestyle factors: Physical activity, Smoking, Alcohol, BMI, Sleep quality Psychological and behavior factors: Catastrophizing, Depression, Kinesiophobia, Distress, Hypervigilance, Self-efficacy, Coping Patients’ beliefs: duration beliefs, Concerns, Treatment beliefs, Therapeutic relation, Identity beliefs
Six weeks follow-up	Pain intensity
Three months follow-up	Pain intensity
Six months follow-up	Pain intensity
Hypothesis 2 There is a clinically meaningful difference between groups with differing level of pain severity (NPRS 1-2 defined mild pain, and NPRS ≥ 3 defined moderate and severe pain) on daily activities, illness perceptions, psychological factors and sleep quality.	
Six weeks follow-up	Symptoms: Disability Psychological factors: Catastrophizing, Depression, Kinesiophobia, Distress, Hypervigilance, Self-efficacy Patients’ beliefs: Concerns, Therapeutic relation, Identity beliefs

Figure 6.1: All variables and their measurement moment for hypothesis 1 and 2.

Quantitative variables and statistical methods

We used the R (version 4.2.2) for the sample size calculation and all analyses.¹⁷ Descriptive statistics to summarize patients’ characteristics were recorded in the analysis tables. The extent of missing data was calculated. Incomplete records at baseline and follow-up were addressed through multiple imputations using full condition specification under the assumption that the data were at least missing at random (MAR).¹⁸ Predictive mean matching was utilized for continuous variables to draw imputations, and logistic regression was used for categorical variables.

Continuous variables were evaluated for normality using Q-Q plots and were expressed as mean with standard deviation (SD) and median with interquartile range (IQR) in both cases of normal and non-normal distribution. Dichotomous and categorical variables were presented using frequencies and percentages. Group differences for all hypotheses were analyzed using the independent-samples T-test for continuous variables that were normally and non-normal distributed; this is acceptable for the large sample size. Chi-square tests were used for categorical and dichotomous variables. Group differences were visualized with histograms and violin plots. The threshold for statistical significance was set at $p < 0.05$.

Due to potential confounding factors across different categories, we conducted linear, logistic, and multinomial regression analyses corresponding to continuous, dichotomous, and categorical outcome measures, respectively, to ensure the robustness of our findings. Multicollinearity was assessed, and variables exhibiting a correlation coefficient higher than 0.8 or a Variance Inflation Factor (VIF) exceeding 5 were excluded from the models.

All variables were adjusted for gender and age. Additionally, each variable was categorized into different subsets of related variables: patients' characteristics, symptoms, lifestyle factors, psychological and behaviour factors, perception factors, and pain intensity at different time points that were measured. This approach allowed us to correct for confounding not only by age and gender but also by other interrelated variables, thereby enhancing the validity of our results.

In cases where the group differ significantly on a variable, we compared the group difference with the minimal detectable change (MDC) and the minimal important change (MIC). The MDC indicates changes that fall outside the measurement error of the health status measurement.¹⁹ The MIC represents the threshold for a minimal within-person change over time, above which patients perceive the changes as meaningful. Assuming all patients have their individual threshold of what they consider a minimal important change, the MIC can be conceptualized as the mean of these individual thresholds.²⁰ However, in this study, differences between groups are assessed and should be interpreted regarding their clinical relevance. If the MDC and/or MIC are available, we will report the specific population on which these values were determined. Additionally, if the difference is lower than the MIC, we will discuss from a clinical perspective whether this difference is clinically meaningful in our specific population.

Results

Participants

In 30 Dutch physiotherapy practices, 2,567 patients were evaluated for eligibility, including 603 participants over a 2.5-year period. 1,600 were primarily excluded due to chronic pain, cervical spine radiculopathy, or widespread pain, and 307 declined to participate. Reasons for declining included lack of interest, scheduling issues, or current stress. Additionally, 58 individuals did not complete the baseline assessment despite signing informed consent and agreeing to participate. For further details, we refer to Appendix 6.3, which contains the study flowchart. The study population included 397 females and 206 men, with an average baseline pain intensity of 5.9 (SD = 1.9) measured on the NPRS and a mean disability score of 2.7 (SD = 2.1) on the Pain Disability Index (PDI). Higher scores on the PDI indicate higher interference of pain with daily activity, where we divided the sum score by the number of completed items (range of 0–7). The final cohort consisted of 198 (33%) individuals experiencing their first episode of (sub)acute neck pain and 405 (67%) with recurrent (sub)acute neck pain. Psychological variables tended towards a non-normal distribution with lower scores. Follow-up losses were significant, with 154 participants not submitting forms by six weeks, increasing to 224 by three months and 231 by six months. At six weeks, 278 of the 449 responders still experienced neck pain, with a mean pain intensity of 4.2 (SD = 2.0); 67 reported mild pain (1–2 on the NPRS), while 209 reported moderate to severe pain (≥ 3 on the NPRS). Of these 278 participants no missing data were detected regarding the variables of interest for the analysis on difference between the two pain intensity groups. The variables exhibited correlations below 0.80 and VIF scores below 2.7, both indicators suggesting minimal multicollinearity and thus reducing concerns about its influence on the regression results.

Hypothesis 1

Table 6.1 details the statistical findings, and corresponding visualizations can be found in Appendix 6.4. Across all measured variables, no statistically significant differences were observed between the patients with a first episode of neck pain and those with a new episode of neck pain in a recurrent pattern on the independent sample T-tests. The variables patients' concerns, treatment beliefs, and therapeutic relations reached a p-value of 0.08, 0.07, and 0.06, respectively. Patient concerns exhibited a mean difference of -0.408 (95% CI: -0.05–0.86), treatment beliefs a

mean difference of -0.22 (95% CI: -0.01–0.45), and ‘therapeutic relation’ showed a mean difference of -0.216 (95% CI: -0.01–0.45) all on a 0–10 point scale. When adjusting for various patients’ beliefs, age and gender in the regression analyses, the differences in treatment beliefs and therapeutic relations were smaller and moved further from statistical significance. Concerns as measured by the IPQ-K, however, reached a statistically significant level ($P = 0.03$) with concerns being higher for the first episode pain group than for the recurrent pain group.

The difference of 0.41 on the concerns scale (0–10) is smaller than the SDC of 0.57, which was determined in a chronic obstructive pulmonary disease (COPD) study sample.²¹ The MIC for this factor has not been established.

Hypothesis 2

Table 6.2 and Figure 6.2 present the analyses’ statistical outcomes and visual representations. The violin plot demonstrated that disability levels for the moderate to severe pain group are more widely distributed compared to the mild pain group, where most patients present with low disability levels. This pattern is also evident for self-efficacy as measured by the PSEQ-2; the moderate to severe pain group displays a broader distribution in self-efficacy scores, whereas most of the mild pain group exhibits high pain self-efficacy scores.

T-tests revealed significant differences in the mean scores of catastrophizing, depression, kinesiophobia, disability, and concerns between the mild and moderate to severe pain group, with the moderate to severe pain group exhibiting higher scores across these factors. Notably, the group with higher pain intensity scored significantly lower on self-efficacy than those with lower pain intensity, with a mean score of -1.25 (95% CI: -1.84–-0.65) on a 0–12 point scale. When adjusting for various psychological factors (see models Table 6.2), age and gender in the regression analyses for catastrophizing, depression, and kinesiophobia, the differences between the two pain groups were smaller in size and no longer showed statistically significant differences.

T-tests and multivariable regression analysis have consistently shown a significant difference in self-efficacy between the pain intensity groups, with scores of 11.2 (SD 1.72) in the mild pain group and 9.97 (SD 2.45) in the higher pain intensity group. These differences persist even after adjusting for various psychological factors, age and gender, demonstrating the robustness of this finding.

Table 6.1: Group difference Recurrent Pain and First Episode Pain Group measured at baseline

Patients characteristics		Recurrent Pain Group Mean (SD) Median (IQR) Number (%)	First Episode Pain Group Mean (SD) Median (IQR) Number (%)	Mean differences continuous variables (95% CI)	Independent sample T-tests P-value	Coefficient (95% CI)	P-value
Symptoms							
Sex							
1 = Male		137 (33.8)	69 (34.8)		0.88	0.03 (-0.33–0.39)	0.87
2 = Female		268 (66.2)	129 (65.2)				
Age		44.4 (15.9) 42 (25)	44.7 (15.1) 45 (25)	-0.33 (-2.44–2.90)	0.84	-1.04 (-3.41–1.33)	0.39
Work status (yes/no)		336 (83.0) 69 (17.0)	172 (86.9) 26 (13.1)		0.26	0.32 (-0.22–0.88)	0.25
Education							
Low level of education		222 (54.8)	99 (50)		0.30	-0.19 (-0.53–0.15)	0.27
High level of education		183 (45.2)	99 (50)				
Symptoms							
Pain intensity at baseline (0–10)		5.88 (1.90) 6 (2)	6.03 (1.80) 6 (2)	-0.15 (-0.16–0.46)	0.34	-0.22 (-0.50–0.06)	0.12
Duration of neck pain Number of weeks		4.52 (2.92) 4 (4)	4.52 (2.92) 4 (4)	0.00 (-0.50–0.50)	0.98	-0.02 (-0.52–0.47)	0.92
Reported pain in different body regions							
No		136 (33.6)	75 (37.9)		0.34	0.18 (-0.18–0.54)	0.32
Yes		269 (66.4)	123 (62.1)				
Accompanying headache							
No		165 (40.7)	84 (42.4)		0.73	0.122–0.14	0.53
Yes		195 (48.1)	89 (44.9)				0.64
I had headache(s) before the neck pain		45 (11.1)	25 (12.6)				
Disability (0–7)		2.77 (2.12) 2.3 (3.1)	2.63 (1.92) 2.1 (2.9)	0.14 (-0.48–0.20)	0.43	0.21 (-0.11–0.52)	0.19

Lifestyle factors					
Physical activity					
Achieving the Dutch Healthy Exercise Norm	144 (35.6)	76 (38.4)	0.56	0.09 (-2.26–0.45)	0.60
Not achieving the Dutch Healthy Exercise Norm	261 (64.4)	122 (61.6)			
Smoking (No/Yes)	357 (88.1) 48 (11.9)	174 (87.9) 24 (12.1)	1.00	-0.06 (-0.26–0.45)	0.82
Alcohol (No/Yes)	87 (21.5) 318 (78.5)	42 (21.2) 156 (78.2)	1.00	0.01 (-0.42–0.42)	0.97
BMI	25.5 (4.33)	25.1 (4.47)	0.26	0.42 (-0.31–1.15)	0.26
Sleep quality					
Sleep quality					
No negative experience with sleeping	93 (23.0)	37 (18.7)	0.27	-0.27 (-0.74–2.22)	0.21
Negative experience with sleeping	312 (77.0)	161 (81.3)			
Psychological factors					
Catastrophizing (0–24)	4.53 (4.49) 3 (6)	4.70 (4.70) 3 (6.75)	0.68	-0.16 (-0.63–0.96)	0.32
Depression (0–21)	2.58 (3.45) 1 (4)	2.25 (3.16) 1 (3)	0.24	0.33 (-0.89–0.22)	0.65
Kinesiophobia (11–44)	16.5 (5.08) 15 (8)	16.7 (5.43) 16 (7.75)	0.57	-0.26 (-0.65–1.17)	0.35
Distress (0–21)	4.56 (4.14) 4 (6)	4.04 (4.07) 3 (5)	0.14	0.52 (-1.22–0.18)	0.32
Hypervigilance (0–80)	31.4 (10.9) 31 (14)	30.2 (12.5) 31 (17)	0.26	1.17 (-3.21–0.88)	0.19
Self-efficacy (0–12)	10.4 (2.29) 11 (2)	10.2 (2.37) 11 (2)	0.54	0.13 (-0.53–0.26)	0.48

Table 6.1 continues on next page.

Table 6.1: Continued

	Recurrent Pain Group		First Episode Pain Group		Mean differences continuous variables (95% CI)	Independent sample T-tests		P-value
	Mean (SD)	Median (IQR)	Mean (SD)	Median (IQR)		P-value	Coefficient (95% CI)	
Coping								
Passive coping	84 (20.7)		38 (19.2)			0.74	-0.07 (-0.53-0.37)	0.75
Active coping	321 (79.3)		160 (80.8)					
Perception factors								
Duration beliefs (0-10)	4.15 (2.68)		4.06 (2.59)		0.09 (-0.54-0.36)	0.70	0.22 (-0.18-0.62)	0.28
	3 (4)		3 (4)					
Concerns (0-10)	3.82 (2.60)		4.23 (2.69)		-0.41 (-0.05-0.86)	0.08	-0.46 (-0.86-0.06)	0.03*
	4 (4)		4 (4)					
Treatment beliefs (0-10)	7.72 (2.00)		7.99 (1.57)		-0.27 (-0.02-0.57)	0.07	-0.11 (-0.37-0.15)	0.42
	8 (2)		8 (2)					
Therapeutic relation (0-10)	8.73 (1.46)		8.94 (1.28)		-0.22 (-0.01-0.45)	0.06	-0.12 (-0.31-0.07)	0.22
	9 (2)		9 (2)					
Identity beliefs (0-10)	6.13 (2.41)		6.07 (2.24)		0.06 (-0.45-0.33)	0.76	0.16 (-0.23-0.56)	0.41
	7 (3)		6 (3)					
Outcomes								
Pain at 6 weeks	2.54 (2.62)		2.55 (2.62)		-0.01 (-0.44-0.46)	0.97	0.05 (-0.33-1.15)	0.78
	2 (4)		2 (5)					
Pain at 3 months	2.00 (2.63)		2.16 (2.70)		-0.16 (-0.30-0.62)	0.49	-0.19 (-0.43-0.44)	0.30
	0 (4)		0 (4)					
Pain at 6 months	1.23 (2.27)		1.29 (2.50)		-0.06 (-0.36-0.48)	0.77	-0.11 (-0.44-0.21)	0.49
	0 (1)		0 (1)					
Chronic pain								
No	362 (89.4)		179 (90.4)			0.80	0.77 (-0.21-1.84)	0.14
Yes	43 (10.6)		19 (9.6)					

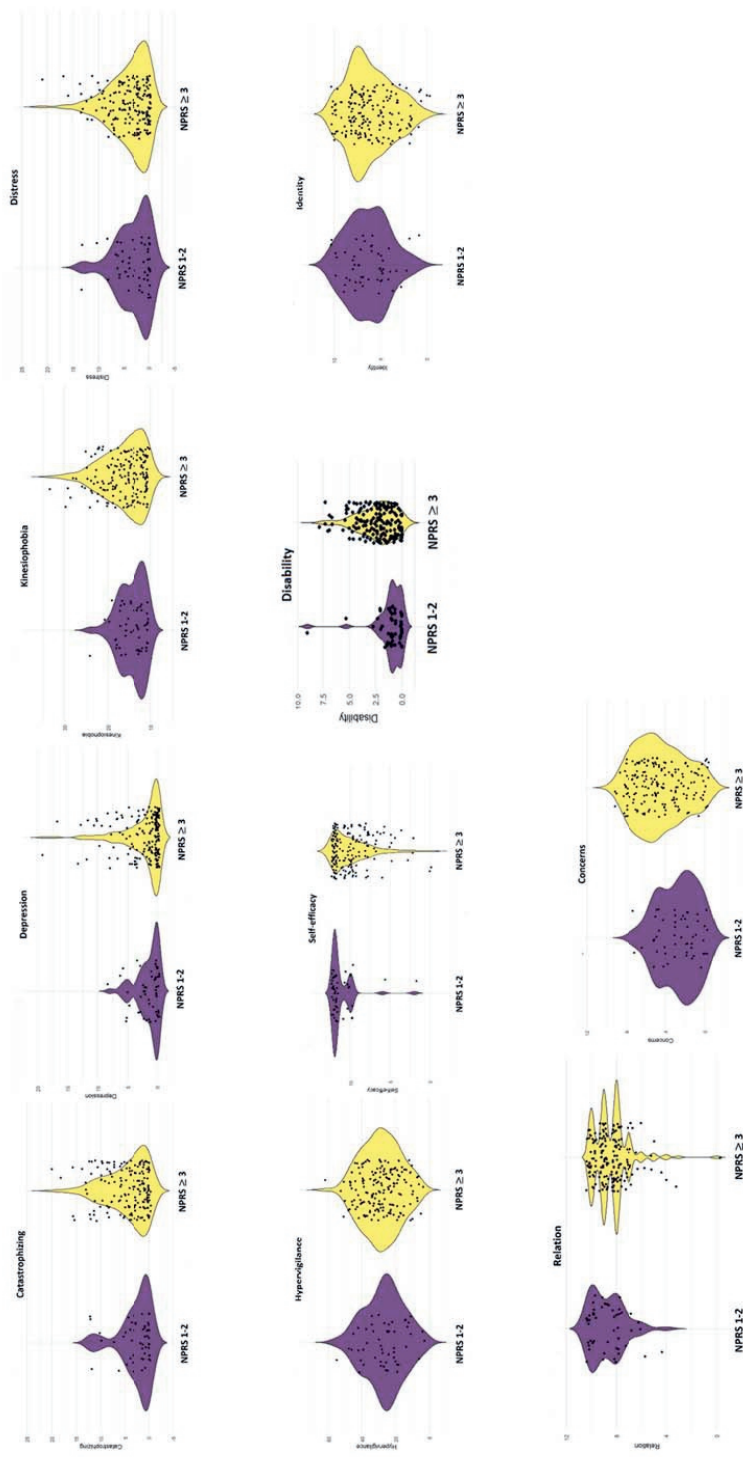


Figure 6.2: Visualization of the Difference in pain severity interference with daily activities, illness perceptions, psychological factors, and sleep quality between pain group measured at 6 weeks follow-up.

Table 6.2: Difference interference pain severity with daily activities, patients’ beliefs and psychological factors at 6 weeks

	Mild pain		Moderate and severe pain		Mean differences (95% CI)	Independent sample T-tests		P-value	Coefficient (95% CI)	P-value
	Mean (SD)	Median (IQR)	Mean (SD)	Median (IQR)		P-value				
Model Psychological and behavior factors										
Catastrophizing (0–24)	2.69 (3.36) 1 (4)		4.43 (4.33) 3 (6)		1.74 (0.61–2.87)	0.003		0.36 (-0.62–1.33)	0.47	
Depression (0–21)	1.5 (2.00) 1 (2)		2.52 (3.66) 1 (3)		0.81 (0.06–1.56)	0.03*		0.11 (0.55–0.79)	0.73	
Kinesiophobia (11–44)	14.4 (3.08) 13 (5)		16.3 (4.76) 15 (7)		1.88 (0.77–2.98)	0.001**		0.66 (-0.39–1.70)	0.22	
Distress (0–21)	3.08 (3.35) 2 (5)		3.89 (3.93) 3 (5)		0.82 (-0.28–1.91)	0.14		-0.13 (-0.92–0.67)	0.75	
Hypervigilance (0–80)	26.7 (11.70) 26 (14.2)		28.8 (14.40) 29 (16.2)		2.11 (-1.54–5.75)	0.09		-0.50 (-3.44–2.43)	0.73	
Self-efficacy (0–12)	11.2 (1.72) 12 (1.25)		9.97 (2.45) 10.5 (3)		-1.25 (-1.84–0.65)	< 0.001***		-0.86 (-1.55–0.17)	0.02*	

Model Disability					
Disability range	1.03 (1.46) 0.9 (1.05)	2.36 (1.78) 2.1 (2.42)	1.33 (0.84–1.81)	< 0.001***	-1.34 (-1.88–0.81) < 0.001***
Model Patients' beliefs					
Concerns range	2.71 (1.96) 2 (3.25)	4.58 (2.49) 5 (4)	1.87 (1.21–2.52)	< 0.001***	-1.84 (-2.57–1.10) < 0.001***
Therapeutic relation range	8.71 (1.38) 9 (2)	8.39 (1.43) 8.5 (1)	-0.43 (-0.76–0.11)	0.14	-0.16 (-0.60–0.28) 0.47
Identity beliefs range	6.35 (2.23) 6.5 (3)	6.18 (2.42) 7 (3)	0.17 (-0.88–0.54)	0.64	0.14 (-0.90–0.62) 0.72

Significance codes: 0 '***' 0.001 '**' 0.01 '*'.

Dependent variable: Model 1 Psychological factors: Catastrophizing, Depression, Kinesiophobia, Distress, Hypervigilance, Self-efficacy. Model 2 Disability: Disability, Model 3 Perceptions: identity beliefs, therapeutic relation, concerns about recovery.

Independent variable: Mild / Moderate to Severe Pain intensity.

Patients with higher pain intensity also reported significantly greater disability and concern levels, with a mean difference of 1.33 (95% CI: 0.84–1.81) on a seven-point disability scale and a two-point higher concern level on a 10-point scale, remaining significant after adjusting for age and gender. Despite these differences, disability levels were relatively low, with mean scores of 0.99 (SD 1.43) for the mild pain group and higher for the moderate to severe pain group 2.31 (SD 1.84). Concern levels score 2.71 (SD 1.96) for mild pain and 4.46 (SD 2.39) for higher pain, was unaffected by adjustments for therapeutic relation, identity beliefs, age and gender.

There is no MDC available for the short form of the PSEQ. The difference of 1.25 (SD 1.84 to 0.65) in self-efficacy is higher than the MIC of -0.5 for patients who score high on the 2-item questionnaire, determined in a study population of patients with chronic low back pain.²² The group that scores higher on the PSEQ-2 in that study is comparable with our study population scores.

The MDC for the PDI was 17.9 points, which, when adjusted for the total score divided by the number of items completed, corresponds to 2.6 points.²³ These findings are based on a study population with a much higher level of disability among musculoskeletal pain patients presenting at secondary care facilities.²³ This is higher than our pain groups' 1.33 (SD 0.84–1.81) difference. However, the MIC value of 9.5, corresponding to 1.4 points when divided, is close to our observed difference.

The difference of 1.87 in illness perception concerns between the pain groups exceeds the SDC of 0.57, indicating a 'real difference' between the groups established on a COPD study population.²¹ However, no MIC is available to address the illness perception 'concerns'.

Discussion

This study found nearly no significant differences between the clinical characteristics of patients experiencing a first episode of NSNP and those with a new episode in a recurrent pattern, nor were differences observed in their six-week, three-month, and six-month recovery rates in primary physiotherapy care. Despite finding statistically significant differences in the T-tests, these differences are negated in regression analyses where confounding variables were considered. Only patients' concerns remained significantly different between these groups. Where patients with a first episode of neck pain experienced more concerns

than the group of patients with neck pain in a recurrent pattern. However, more significant differences were observed in the interference of pain severity – mild pain (1–2 NPRS) and moderate to severe pain (≥ 3 NPRS) – with daily activities (disability), patients' concerns, and self-efficacy. We observed a 1.33-point (SD 0.84–1.81) difference in disability on a 0–7 point scale, a 1.25-point (SD -1.84 to -0.65) difference in self-efficacy on a 0–12 scale, and a 1.87-point (SD 1.21–2.52) difference on patients' concerns a 0–10 scale. Whether these significant results can be considered clinically meaningful will now be discussed.

The absence of an established MDC for the Pain Self-Efficacy Questionnaire-2 (PSEQ-2) raises concerns about accurately measuring the observed 1.25-point difference in self-efficacy at the group level. Additionally, the PSEQ-2's significant ceiling effect limits its ability to differentiate among patients with high self-efficacy.²⁴ Our study population exceeded a score of 10, suggesting these limitations might affect our study outcome. It may not have been the optimal measurement tool for this study population. Although the difference is higher than the MIC of -0.5 for high-scoring populations, the absence of the MDC makes the interpretation difficult. However, knowing this tool has an evident ceiling effect, a 1.25-point difference on a 0–12 scale can be seen as clinically meaningful.

The MDC for the Pain Disability Index (PDI) is higher than the observed difference between our pain groups. However, the MIC is close to our observed difference, with a discrepancy of only 0.07 points. These findings are based on a population with a higher level of disability than ours.²³ The reference PDI value for patients with painful musculoskeletal and spinal disorders is 37.8 ± 14.2 (5.4 when divided by 7 completed items), much higher than the 0.99 (SD 1.43) for our mild pain group and 2.31 (SD 1.84) for our moderate to severe pain group.²⁵ A bottom effect may influence our study population. Thus, in a population with relatively low disability compared to other subgroups where the MDC and MIC are based, a difference of 1.33 points in our study can be considered clinically meaningful.

The difference in patient concerns exceeds the MDC, although no established MIC exists.²¹ We observed a 2-point difference on a 0–10 scale, from relatively mild concerns (2.61, SD 1.90) in the mild pain group to moderate concerns (4.49, SD 2.52) in the moderate-to-severe pain group. This evident difference indicates a clinically meaningful difference concern with higher pain intensity. In contrast, the difference between first-episode and recurrent acute pain patients is only 0.4 on the same scale, which is below the MDC and can be considered not clinically meaningful.

Strengths and limitations

When treatment beliefs and therapeutic relations variables were adjusted for patients' concerns, age and gender, the differences between the two pain groups moved away from statistical significance in the initial T-tests. Similarly, after adjusting for various psychological factors in the regression analyses – specifically catastrophizing, depression, and kinesiophobia – the differences between the pain groups decreased to not statistically significant. This suggests that the variability in these variables may be more influenced by other factors than by pain intensity alone. The initial findings of significant differences in the unadjusted results from the T-tests might oversimplify more complex interrelations between psychological factors and experienced pain. Suggesting that at least a part of the differences can be explained by potential confounders. Correcting and further analyzing these differences is crucial and represents a strength of this study, as it aids in demonstrating actual differences between the groups. Notably, after adjustments for various beliefs, psychological factors, age, and gender, the differences in patients' concerns, self-efficacy, and disability remained significant, underscoring the robustness of these findings.

Interrelationships

The potential complex interrelations between psychological factors, illness perceptions, and experienced pain intensity become apparent in the data analysis of this study. These factors are known to often be highly correlated²⁶ and/or likely have common underlying, or at least partly overlapping, constructs.^{27,28} Catastrophizing, defined as an exaggerated and negative cognitive-emotional schema activated during actual or anticipated painful stimulation, was originally described as a maladaptive cognitive style prevalent among patients with anxiety and depressive disorder. Catastrophizing and kinesiophobia are closely related, whereas catastrophizing often leads to increased kinesiophobia, suggesting that negative perceptions of pain contribute to a heightened fear of movement.²⁹ While catastrophizing is a broader tendency to respond negatively to pain, kinesiophobia specifically focuses on the fear of movements that could exacerbate pain.²⁹

Operational and conceptual confounding presents interpretive challenges among these variables. Depression and catastrophizing often co-occur in patients with chronic pain, with catastrophizing more directly linked to the anticipation and experience of pain, whereas depression encompasses a broader range of emotional and affective symptoms.²⁸

Significant overlap exists between kinesiophobia and catastrophizing; both are associated with negative emotional reactions to pain and are linked to adverse illness perceptions, suggesting that these cognitions together constitute a domain of negative emotional cognitions. Established relationships between various cognitive concepts have shown that self-efficacy is associated with fear-avoidance cognitions and catastrophizing in individuals with chronic pain.^{27,30,31}

Despite self-efficacy, cognitive coping styles, fear-avoidance cognitions, and illness beliefs being considered theoretically distinct entities, empirical evidence and theoretical similarities suggest considerable overlap among these concepts. In clinical practice, the interaction between catastrophizing, kinesiophobia, distress, depression, self-efficacy, and illness beliefs must be taken into account when interpreting patients' clinical presentations and exploring treatment possibilities and limitations.³² It is expected that not only one factor shows higher scores.

Considering this, whether we categorized the different variables in the correct models for regression analyses can be questioned. Psychological factors and illness perceptions are interrelated.³¹ Consequently, the confounding effect of factors in different models can be overlooked, potentially obscuring the true differences between the two pain intensity groups.

Practical guidelines

The current Dutch guideline categorizes patients with neck pain into treatment profiles based on the course of their condition: (1) normal course, (2) delayed course without dominant psychosocial influences, and (3) delayed course with dominant psychosocial influences. Recurrent neck pain is typically assigned to the delayed category.^{33,34} However, our findings indicate that patients with recurrent episodes of neck pain, who exhibit baseline characteristics similar to those experiencing their first episode, might be more accurately grouped with the normal course category. This study primarily focused on perceptual, psychological, and disability factors and did not explore biological differences such as muscle strength, endurance, and cervical mobility, which could be important in refining these classifications. Moreover, international physical therapy guidelines do not reflect this distinction in different pain courses.³⁵ This discrepancy suggests that guideline developers should consider the current classification system, possibly by integrating clearly defined neck pain stages and a broader range of clinical factors.

Research implications

In our earlier prognostic study, we used NPRS 3, a common cut-off point, to identify patients in the chronic pain group.^{36–38} However, the minimal differences we observed raise questions about the correctness of this threshold. Its arbitrary nature suggests that alternative thresholds might yield different outcomes. This underscores the need for further research to establish a more clinically relevant cut-off point that could inform prognostic research and the WHO's ICD-11 guidelines for diagnosing chronic primary pain, which currently recommends including NRS scores for pain, disability and distress without specifying a mandatory threshold.⁷ Moreover, this study highlighted that pain of low intensity is correlated with lower disability and psychological impact, contrasting with chronic pain patients who often exhibit higher scores in these areas.^{10–12} Given that chronic pain is defined as pain in one or more anatomical regions accompanied by significant emotional distress or functional disability, the inclusion criteria and outcome measures in future studies might benefit from a revised cut-off point that better reflects the impact on emotional well-being and disability.

Most studies, including our prognostic study, traditionally focus on pain intensity. However, we advocate for a higher threshold for pain intensity, considering also the associated emotional and functional impairments. Establishing a more nuanced cut-off point for pain intensity in future research could enhance the accuracy of outcome or inclusion criteria, aligning them more closely with the multifaceted impacts of chronic pain.

Conclusion

There are no significant or clinically meaningful differences in clinical characteristics or pain recovery rates between a first-episode pain period and pain in a recurrent patron in NSNP. Significant differences exist in the impact of pain severity on daily activities, patient concerns, and self-efficacy. We considered the differences as clinically meaningful.

Key points

- The clinical characteristics of patients with acute nonspecific neck pain (NSNP) closely align with those experiencing a new episode of acute NSNP in a recurrent pattern.
- There are no significant differences in the pain recovery rates between patients experiencing a first episode of NSNP and those with a new episode of acute neck pain in a recurrent pattern.
- Significant and clinically meaningful differences exist in the extent to which pain severity, categorized as mild pain (1–2 NPRS) and moderate to severe (≥ 3 NPRS), interferes with daily activities, patient concerns, and self-efficacy.
- When determining whether a difference between groups is clinically meaningful, using a combination of the MIC, the MDC, a critical examination of the different populations in the studies, and clinical expertise is important.

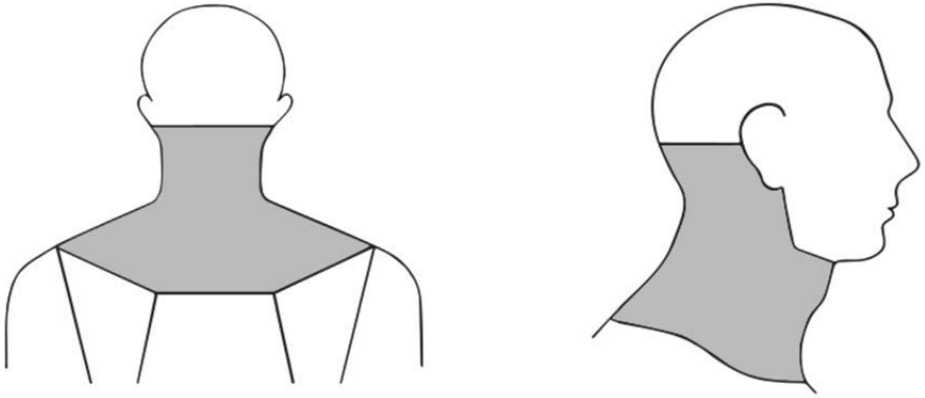
References

1. Childs JD, Fritz JM, Piva SR, et al. Proposal of a classification system for patients with neck pain. *Journal of Orthopaedic and Sports Physical Therapy*. 2004;34:686–96. doi: 10.2519/jospt.2004.1451
2. Ishaq I, Mehta P, Skinner IW, et al. Treatment classifications and interventions for neck pain: a scoping review. *J Clin Epidemiol*. 2023;159:1–9. doi: 10.1016/j.jclinepi.2023.04.010
3. Damgaard P, Bartels EM, Ris I, et al. Evidence of Physiotherapy Interventions for Patients with Chronic Neck Pain: A Systematic Review of Randomised Controlled Trials. *ISRN Pain*. 2013;2013:1–23. doi: 10.1155/2013/567175
4. Tsakitzidis G, Remmen R, Dankaerts W, et al. Non-specific neck pain and evidence-based practice. *Eur Sci J*. 2013;9.
5. Fairbank J, Gwilym SE, France JC, et al. The Role of Classification of Chronic Low Back Pain. *Spine (Phila Pa 1976)*. 2011;36:S19–42. doi: 10.1097/BRS.0b013e31822ef72c
6. Smith BH, Fors EA, Korwisi B, et al. The IASP classification of chronic pain for ICD-11: applicability in primary care. *Pain*. 2019;160:83–7. doi: 10.1097/j.pain.0000000000001360
7. Nicholas M, Vlaeyen JWS, Rief W, et al. The IASP classification of chronic pain for ICD-11: chronic primary pain. *Pain*. 2019;160:28–37. doi: 10.1097/j.pain.0000000000001390
8. Hay G, Korwisi B, Rief W, et al. Pain severity ratings in the 11th revision of the International Classification of Diseases: a versatile tool for rapid assessment. *Pain*. 2022;163:2421–9. doi: 10.1097/j.pain.0000000000002640
9. Treede R-D, Rief W, Barke A, et al. A classification of chronic pain for ICD-11. *Pain*. 2015;156:1003–7. doi: 10.1097/j.pain.0000000000000160
10. Miró J, de la Vega R, Solé E, et al. Defining mild, moderate, and severe pain in young people with physical disabilities. *Disabil Rehabil*. 2017;39:1131–5. doi: 10.1080/09638288.2016.1185469
11. Gerhart JI, Burns JW, Bruehl S, et al. Variability in negative emotions among individuals with chronic low back pain: relationships with pain and function. *Pain*. 2018;159:342–50. doi: 10.1097/j.pain.0000000000001102
12. Woby SR, Roach NK, Urmston M, et al. The relation between cognitive factors and levels of pain and disability in chronic low back pain patients presenting for physiotherapy. *European Journal of Pain*. 2007;11:869–77. doi: 10.1016/j.ejpain.2007.01.005
13. Verwoerd MJ, Wittink H, Maissan F, et al. A study protocol for the validation of a prognostic model with an emphasis on modifiable factors to predict chronic pain after a new episode of acute- or subacute nonspecific idiopathic, non-traumatic neck pain presenting in primary care. *PLoS One*. 2023;18:e0280278. doi: 10.1371/journal.pone.0280278
14. von Elm E, Altman DG, Egger M, et al. The Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) statement: guidelines for reporting observational studies. *J Clin Epidemiol*. 2008;61:344–9. doi: 10.1016/j.jclinepi.2007.11.008
15. Innovero Software Solutions B.V. Formdesk. en.formdesk.com.
16. Thoomes EJ, van Geest S, van der Windt DA, et al. Value of physical tests in diagnosing cervical radiculopathy: a systematic review. *Spine Journal*. 2018;18:179–89. doi: 10.1016/j.spinee.2017.08.241
17. R Core Team. A Language and Environment for Statistical Computing. 2018.

- 18 Pedersen A, Mikkelsen E, Cronin-Fenton D, et al. Missing data and multiple imputation in clinical epidemiological research. *Clin Epidemiol.* 2017;Volume 9:157–66. doi: 10.2147/CLEP.S129785
- 19 de Vet HC, Terwee CB, Ostelo RW, et al. Minimal changes in health status questionnaires: distinction between minimally detectable change and minimally important change. *Health Qual Life Outcomes.* 2006;4:54. doi: 10.1186/1477-7525-4-54
- 20 Terwee CB, Peipert JD, Chapman R, et al. Minimal important change (MIC): a conceptual clarification and systematic review of MIC estimates of PROMIS measures. *Quality of Life Research.* 2021;30:2729–54. doi: 10.1007/s11136-021-02925-y
- 21 de Raaij EJ, Schröder C, Maissan FJ, et al. Cross-cultural adaptation and measurement properties of the Brief Illness Perception Questionnaire-Dutch Language Version. *Man Ther.* 2012;17:330–5. doi: 10.1016/j.math.2012.03.001
- 22 Chiarotto A, Vanti C, Cedraschi C, et al. Responsiveness and Minimal Important Change of the Pain Self-Efficacy Questionnaire and Short Forms in Patients With Chronic Low Back Pain. *J Pain.* 2016;17:707–18. doi: 10.1016/j.jpain.2016.02.012
- 23 Soer R, Köke AJA, Vroomen PCAJ, et al. Extensive Validation of the Pain Disability Index in 3 Groups of Patients With Musculoskeletal Pain. *Spine (Phila Pa 1976).* 2013;38:E562–8. doi: 10.1097/BRS.0b013e31828af21f
- 24 Dubé M-O, Langevin P, Roy J-S. Measurement properties of the Pain Self-Efficacy Questionnaire in populations with musculoskeletal disorders: a systematic review. *Pain Rep.* 2021;6:e972. doi: 10.1097/PR9.0000000000000972
- 25 Soer R, Köke AJA, Speijer BLGN, et al. Reference Values of the Pain Disability Index in Patients With Painful Musculoskeletal and Spinal Disorders. *Spine (Phila Pa 1976).* 2015;40:E545–51. doi: 10.1097/BRS.0000000000000827
- 26 Campbell P, Bishop A, Dunn KM, et al. Conceptual overlap of psychological constructs in low back pain. *Pain.* 2013;154:1783–91. doi: 10.1016/j.pain.2013.05.035
- 27 de Rooij A, Steultjens MP, Siemonsma PC, et al. Overlap of cognitive concepts in chronic widespread pain: An exploratory study. *BMC Musculoskelet Disord.* 2011;12:218. doi: 10.1186/1471-2474-12-218
- 28 Sullivan MJ, D'Eon JL. Relation between catastrophizing and depression in chronic pain patients. *J Abnorm Psychol.* 1990;99:260–3. doi: 10.1037/0021-843X.99.3.260
- 29 Varallo G, Suso-Ribera C, Ghiggia A, et al. Catastrophizing, Kinesiophobia, and Acceptance as Mediators of the Relationship Between Perceived Pain Severity, Self-Reported and Performance-Based Physical Function in Women with Fibromyalgia and Obesity. *J Pain Res.* 2022; 15:3017–29. doi: 10.2147/JPR.S370718
- 30 Denison E, Åsenlöf P, Sandborgh M, et al. Musculoskeletal Pain in Primary Health Care: Subgroups Based on Pain Intensity, Disability, Self-Efficacy, and Fear-Avoidance Variables. *J Pain.* 2007;8:67–74. doi: 10.1016/j.jpain.2006.06.007
- 31 van Ittersum MW, van Wilgen CP, Hilberdink WKHA, et al. Illness perceptions in patients with fibromyalgia. *Patient Educ Couns.* 2009;74:53–60. doi: 10.1016/j.pec.2008.07.041
- 32 Nicholas MK, Linton SJ, Watson PJ, et al. Early Identification and Management of Psychological Risk Factors (“Yellow Flags”) in Patients With Low Back Pain: A Reappraisal. *Phys Ther.* 2011;91:737–53. doi: 10.2522/ptj.20100224
- 33 Bier JD, Scholten-Peeters WGM, Staal JB, et al. Clinical Practice Guideline for Physical Therapy Assessment and Treatment in Patients With Nonspecific Neck Pain. *Phys Ther.* 2018;98:162–71. doi: 10.1093/ptj/pzx118

- 34 Bier JD, Scholten-Peeters GGM, Staal JB, Pool J, van Tulder M, Beekman E, Meerhoff GM, Knoop J, Verhagen AP. KNGF-richtlijn Nekpijn Verantwoording en toelichting. 2016.
- 35 Neck Pain Guidelines: Revision 2017: Using the Evidence to Guide Physical Therapist Practice. *Journal of Orthopaedic & Sports Physical Therapy*. 2017;47:511–2. doi: 10.2519/jospt.2017.0507
- 36 Woo A, Lechner B, Fu T, et al. Cut points for mild, moderate, and severe pain among cancer and non-cancer patients: a literature review. *Ann Palliat Med*. 2015;4:176–83.
- 37 Boonstra AM, Stewart RE, Albère AJ, et al. Cut-offpoints for mild, moderate, and severe pain on the numeric rating scale for pain in patients with chronic musculoskeletal pain: Variability and influence of sex and catastrophizing. *Front Psychol*. 2016;7. doi: 10.3389/fpsyg.2016.01466
- 38 Hirschfeld G, Zernikow B. Variability of ‘optimal’ cut points for mild, moderate, and severe pain: neglected problems when comparing groups. *Pain*. 2013;154:154–9. doi: 10.1016/j.pain.2012.10.008
- 39 Hill J, Lewis M, Papageorgiou AC, et al. Predicting Persistent Neck Pain: A 1-year follow-up of a population cohort. *Spine (Phila Pa 1976)*. 2004;29:1648–54. doi: 10.1097/01.BRS.0000132307.06321.3C

Appendix 6.1: Anatomic region neck pain³⁹



Appendix 6.2: Variables and their measurement method

Variables	Measure and Range of the Scale	Hypothesis
Patients' characteristics		
Sex	Self-report question (Male/Female)	1
Age	Self-report question	1
Work status	Self-report question (Yes/No)	1
Education	Self-report question different education levels. Categorized in low level and high level of education.	1
Symptoms		
Pain intensity at baseline	Numeric Pain Rating Scale (NPRS) Range 0–10 "On a scale of 0 to 10, how much pain do you experience? Where 0 is no pain at all and 10 is the most imaginable pain"	1
Duration of neck pain	Number of weeks	1
Reported pain in different body regions	Self-report question: Do you also experience pain in other parts of your body? (yes/no)	1
Accompanying headache	Self-report question: Have you experienced accompanying headache(s) since you have neck pain? Yes / No/ I had headache(s) before the neck pain.	1
Disability	Pain Disability Index (PDI) is a 7-item Pain Disability Index (PDI) is a 7-item questionnaire to investigate the magnitude of self-reported pain-related disability. The PDI measures family/home responsibilities, recreation, social activity, occupation, sexual behavior, self-care, and life support. Higher scores indicate higher interference of pain with daily activity. The sum score will be divided by the entered items (range of 0–7)	1 and 2
Lifestyle factors		
Physical activity	Measured by the activity level according to the Dutch Healthy Exercise Norm. Dived into three categories: (1) I don't move 30 minutes any day a week of moderate intensity. (2) I'm exactly in between one and three (3) I am five days or more active per week	1
Smoking	Self-report question: Do you smoke? (Yes/No)	1
Alcohol	Self-report question: Do you drink alcohol? (Yes/No)	1
BMI	Self-report question: What is your height? And what is your weight? Body Mass Index (BMI): weight/(length x length in meters)	1

Appendix 6.2 continues on next page.

Appendix 6.2: Continued

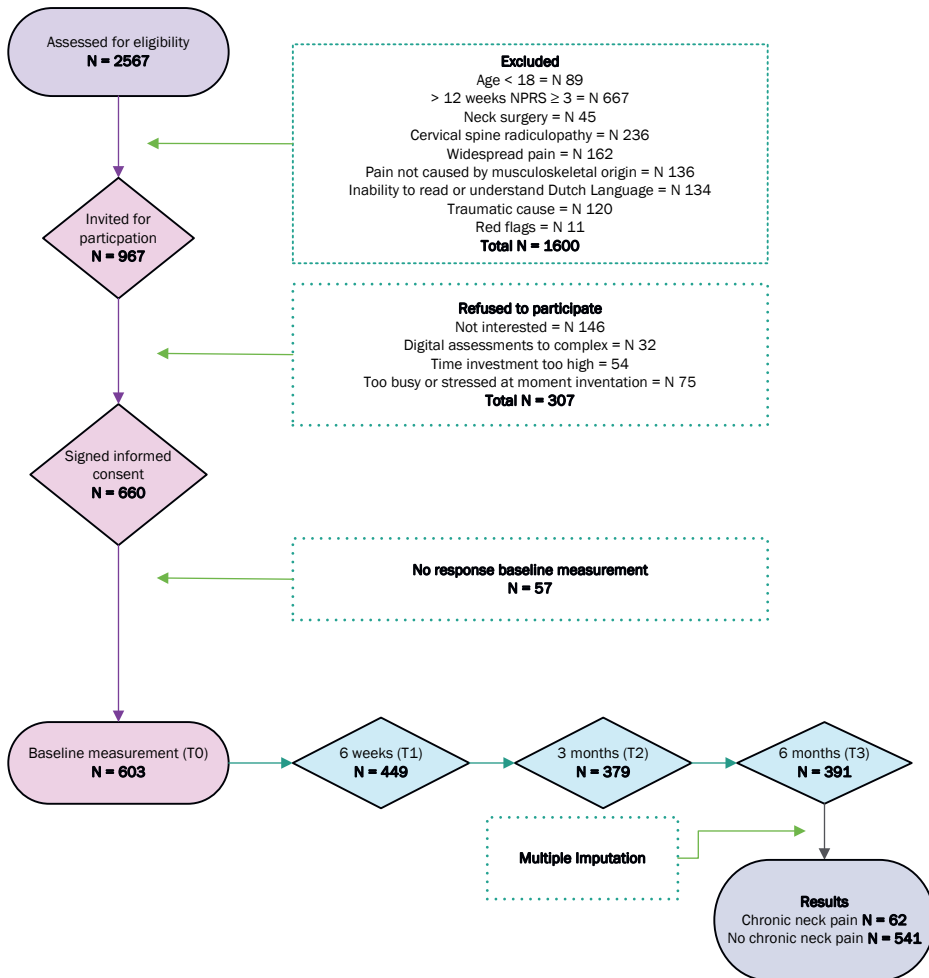
Variables	Measure and Range of the Scale	Hypothesis
Sleep quality		
Sleep quality	Adjusted sleep quality question from the Neck Disability Index (NDI) and is subdivided in 4 domains; (1) wake up rested, (2) number of hours disturbed while sleeping, (3) fall asleep, and (4) personal experience sleep quality (1) Yes / No (2) 0–5 Higher scores indicate more hours disturbed while sleeping (3) Yes / No difficulty falling asleep (4) Yes / No personal experience difficulty sleeping or falling asleep If all questions are answered with a negative result the participant is indicated with no sleeping problems (wake up rested, no hours disturbed sleeping, no problems falling asleep and experience no sleep problems). If one question is answered positive, the participant is indicated with sleeping problems.	1
Psychological and behavior factors		
Catastrophizing	Pain Catastrophizing Scale (PCS) short version is a 6-item questionnaire that assesses catastrophic thoughts or feelings associated with the experience of pain. Range 0–24. Higher scores indicate more catastrophic thoughts.	1 and 2
Depression	Depression Anxiety Stress Scale 21-item version (DASS-21) Range 0–21, higher scores indicate a higher degree of depression.	1 and 2
Kinesiophobia	Tampa Scale for Kinesiophobia (TSK) 11-item version. Range 11–44, higher scores indicate a higher degree of kinesiophobia.	1 and 2
Distress	Depression Anxiety Stress Scale 21-item version (DASS-21) Range 0–21, higher scores indicate a higher degree of stress.	1 and 2
Hypervigilance	Pain Vigilance Awareness Questionnaire (PVAQ). Range 0–80, higher scores indicate a higher degree of vigilance.	1 and 2
Self-efficacy	Pain Self-efficacy Questionnaire 2-item version. Range 0–12, higher scores indicate a higher degree of self-efficacy.	1 and 2
Coping	Pain Coping Inventory (PCI) is a 33-items questionnaire and is subdivided into six scales: pain transformation, distraction, reducing demands, retreating, worrying, and resting Transforming the classification into an active (pain transformation, distraction and reducing demands) and passive coping strategy (retreating, worrying, resting). Active coping = 12–48. Passive coping = 21–84.	1

Appendix 6.2 continues on next page.

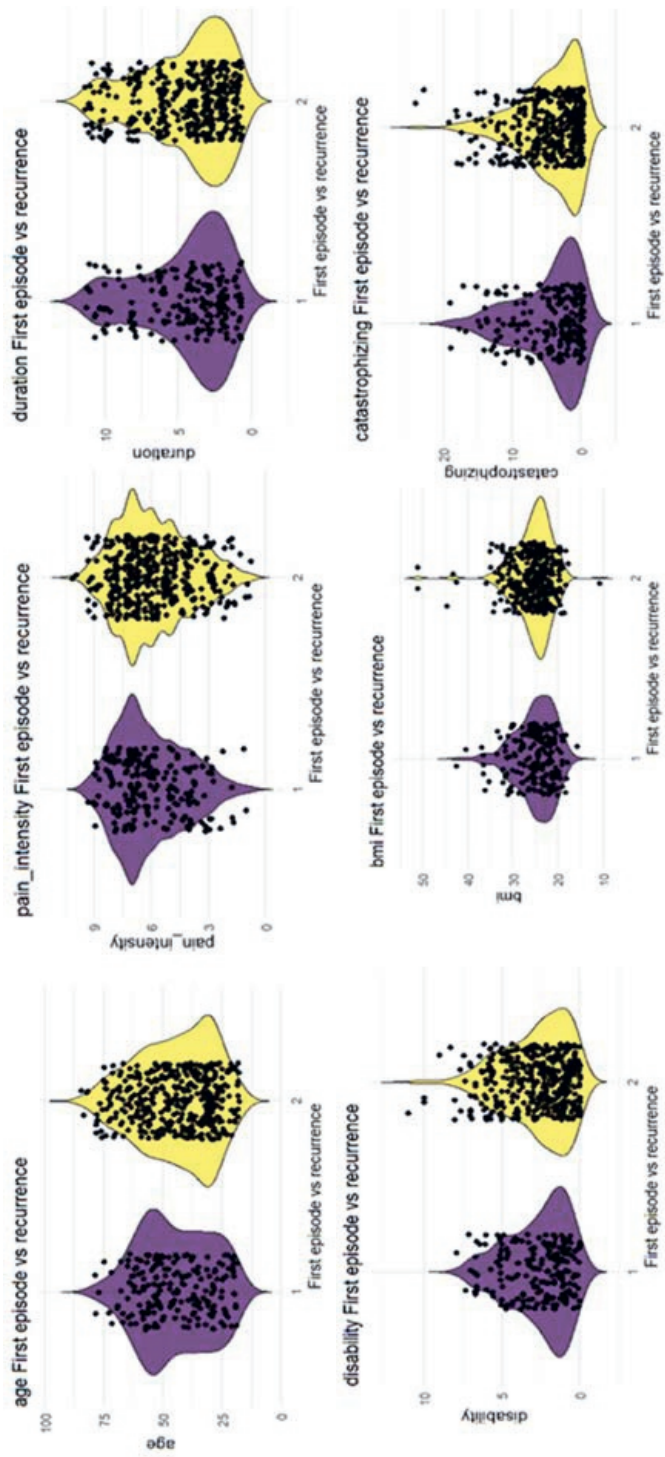
Appendix 6.2: Continued

Variables	Measure and Range of the Scale	Hypothesis
Patients' beliefs		
Duration beliefs	Brief Illness Perception Questionnaire-Dutch language version (IPQ-DLV). How long do you think your neck pain will continue? (0 a very short time – 10 forever) Range 0-10, higher scores indicate a maladaptive illness perception.	1
Concerns	Brief Illness Perception Questionnaire-Dutch language version (IPQ-DLV). How concerned are you about your illness? (0 not at all concerned – 10 extremely concerned). Range 0–10, higher scores indicate a maladaptive illness perception.	1 and 2
Treatment beliefs	Brief Illness Perception Questionnaire-DLV. Single question: How much do you think your treatment can help your neck pain? (0 not at all – 10 extremely helpful) Range 0–10, a lower score indicates a maladaptive illness perception.	1
Therapeutic relation	Self-report question: How much trust do you have in your healthcare provider/ physiotherapist? 0 no trust at all – 10 very much confidence Range 0–10.	1 and 2
Identity beliefs	Brief Illness Perception Questionnaire-DLV Single question: How well do you feel you understand your illness? (0 don't understand at all – 10 understand very clearly). Range 0–10, a lower score indicates a maladaptive illness perception.	1 and 2

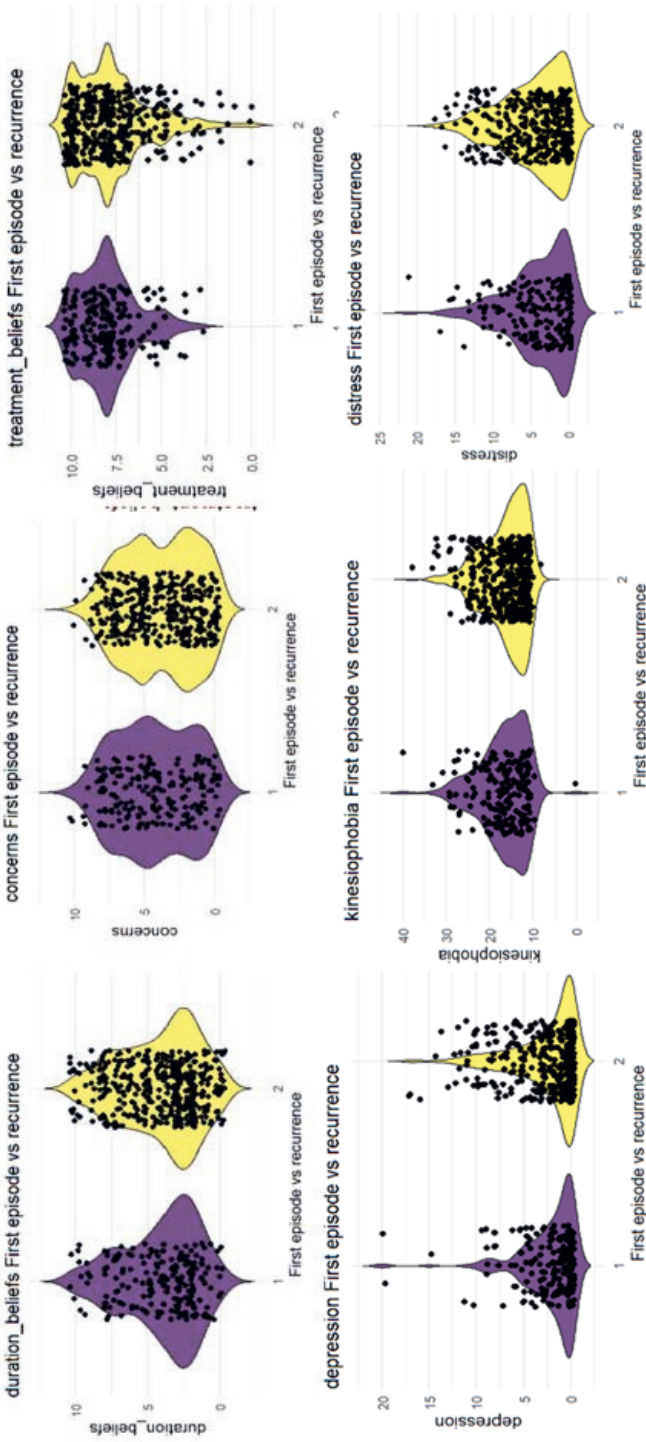
Appendix 6.3: Flow-chart



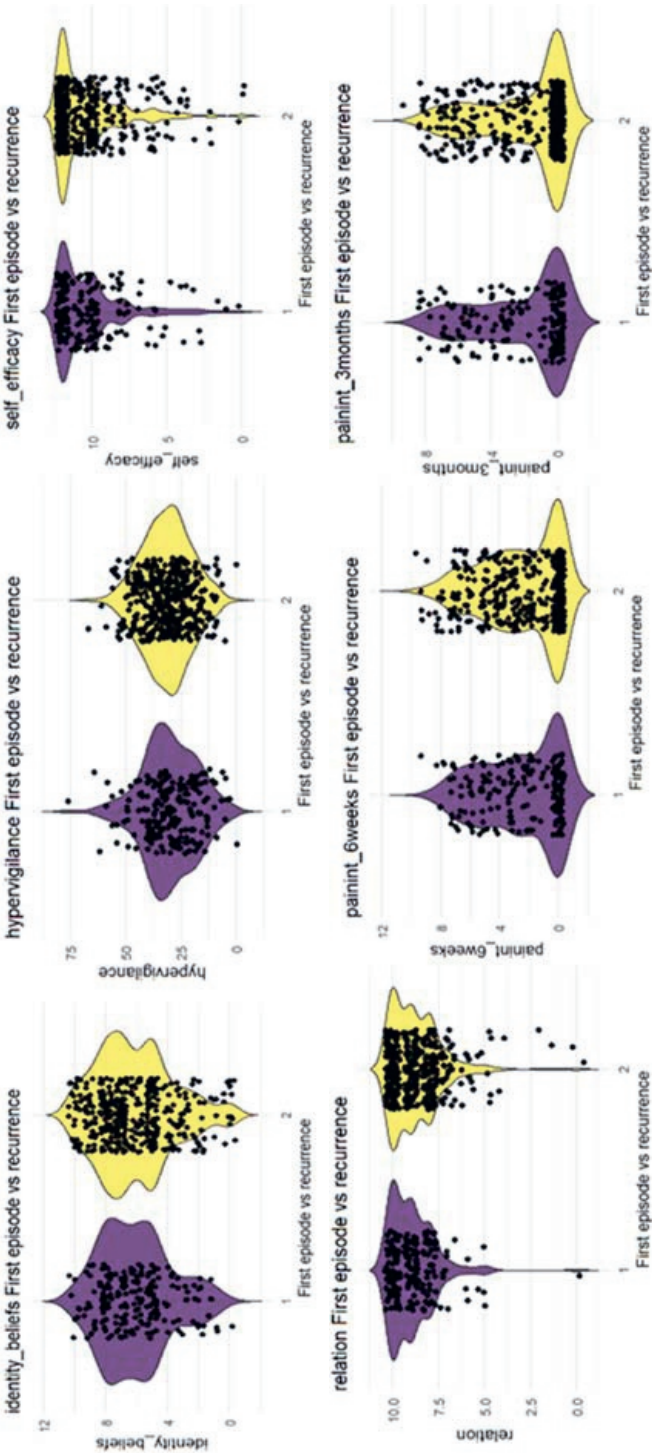
Appendix 6.4: Visualization Group difference Recurrent Pain and First Episode Pain Group



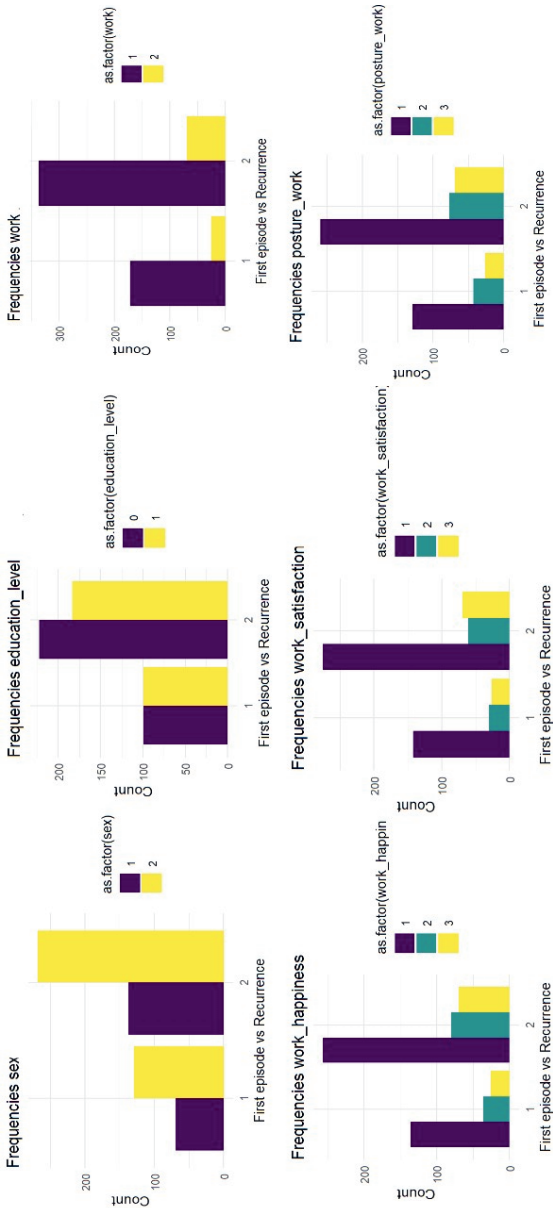
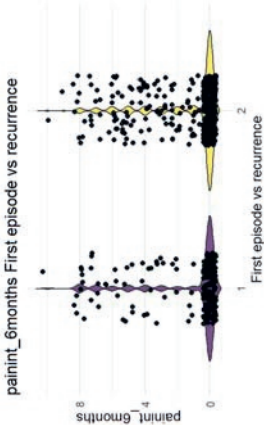
Appendix 6.4: Continued



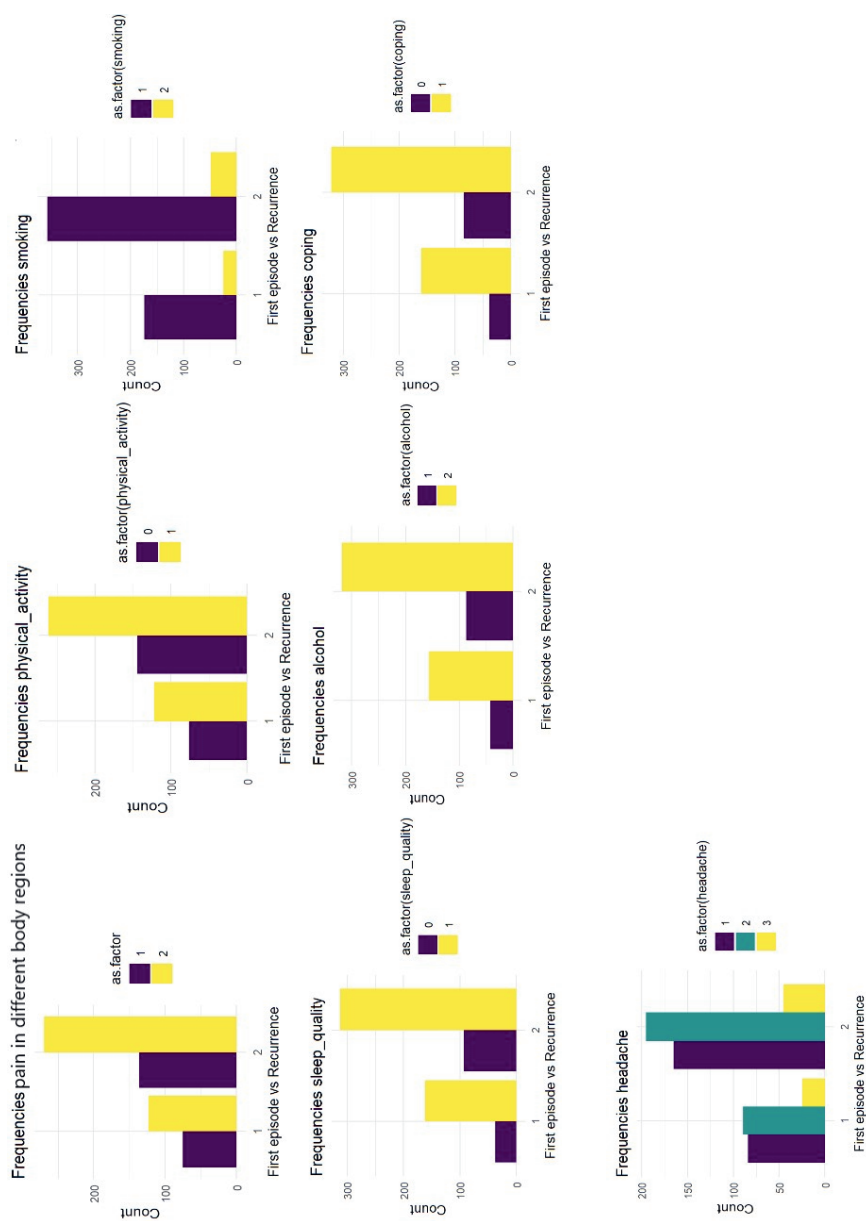
Appendix 6.4: Continued



Appendix 6.4: Continued



Appendix 6.4: Continued



Part 3





Chapter 7

Physiotherapists' knowledge, attitude and practice behavior to prevent chronification in patients with non-specific, non-traumatic, acute and subacute neck pain: a qualitative study

M.J. Verwoerd, H. Wittink, M.E.J.B. Goossens, F. Maissan, R.J.E.M. Smeets

Published Musculoskeletal Science and Practice, 2022, February

Background: The purpose of this study was to explore physiotherapists' knowledge, attitude, and practice behavior in assessing and managing patients with non-specific, non-traumatic, acute and subacute neck pain, with a focus on prognostic factors for chronification.

Method: A qualitative study using in-depth semi-structured interviews was conducted with 13 physiotherapists working in primary care. A purposive sampling method served to seek the broadest perspectives. The knowledge-attitude and practice framework was used as an analytic lens throughout the process. Textual data were analyzed using qualitative content analysis with an inductive approach and constant comparison.

Results: Seven main themes emerged from the data; physiotherapists self-estimated knowledge and attitude, role clarity, therapeutic relationship, internal- and external barriers to practice behavior, physiotherapists' practice behaviors, and self-reflection. These findings are presented in an adjusted knowledge- attitude and practice behavior framework.

Conclusion: A complex relationship was found between a physiotherapist's knowledge about, attitude, and practice behavior concerning the diagnostic process and interventions for non-specific, non-traumatic, acute, and subacute neck pain. Overall, physiotherapists used a biopsychosocial view of patients with non-specific neck pain. Physiotherapists' practice behaviors was influenced by individual attitudes towards their professional role and therapeutic relationship with the patient, and individual knowledge and skills, personal routines and habits, the feeling of powerlessness to modify patients' external factors, and patients' lack of willingness to a biopsychosocial approach influenced physiotherapists' clinical decisions. In addition, we found self-reflection to have an essential role in developing self-estimated knowledge and change in attitude towards their therapeutic role and therapist-patient relationship.

Key words: Non-specific neck pain, physiotherapists attitude, practice behavior

Introduction

Neck pain (NP) is third in the rating of 'years lived with disability' in non-fatal diseases in Europe.¹ NP has a substantial impact on health related quality of life for patients and has significant economic consequences for society.^{2,3} In particular, NP that becomes chronic causes high healthcare costs.⁴ The incidence of NP in the general population is estimated between 15 and 18% per year.^{5,6} In the Netherlands, NP is the most prevalent musculoskeletal disorder presented at physiotherapy practices.⁷ Childs et al. (2008) and others suggest that rates of persistent NP are substantial: 30% of patients with NP will develop chronic symptoms, and 37% of individuals who experience NP will report persistent problems for at least 12 months.^{4,5,8}

Chronic pain interferes considerably with a person's everyday activities, is associated with depressive symptoms, and affects relationships and interactions with others.⁹ The reported effect of physiotherapy treatment of chronic musculoskeletal pain is, at best, only moderate.¹⁰⁻¹² It is therefore important to prevent chronicity and this must preferably occur in the (sub)acute phase of musculoskeletal pain.

It is known that neurophysiological changes responsible for the chronification of pain are modulated by psychosocial factors.¹³ Therefore, to prevent chronification of non-specific acute and subacute, non-traumatic NP, a biopsychosocial view on patients seems important and is recommended by the Dutch Physiotherapy guideline.^{14,15} However, previous research shows that the need to recognize psychosocial disturbances is only partially recognized amongst physiotherapists, and practice behavior often shows that physical problems are prioritized above psychosocial aspects.¹⁶⁻¹⁸ Based on the theoretical Knowledge, Attitude, and Practice (KAP) framework, practice behavior is determined by the knowledge and attitudes about health and illness and directly influences preventive practice.¹⁹ Therefore, the knowledge and attitudes held by physiotherapists likely play a key role in their practice behavior and thus the approach they take in treating their patients. So far physiotherapists' practice behavior has mostly been studied in patients with chronic musculoskeletal complaints.¹⁶ What physiotherapists know about the biomedical and psychosocial aspects in non-specific, acute and subacute NP, and their attitudes and practice behavior is unknown, however.

Therefore, the purpose of this qualitative study is to explore physiotherapists' knowledge, attitude, and practice behavior in assessing and managing patients

with non-specific, non-traumatic, acute and subacute NP with a specific focus on how they identify and try to modify prognostic factors for chronification in these patients.

Methods

This qualitative study using semi-structured interviews with physiotherapists working in primary care and was conducted and reported according to the COREQ 32-item checklist for Qualitative studies to strengthen rigor and comprehensiveness (Appendix 7.1).²⁰

Participant selection

The inclusion criteria were that participants are working in primary care, with a minimum of one year of work experience, and dealing with at least one patient with non-specific NP per week. These inclusion criteria and purposive sampling were employed for maximum variance based on sex, age, clinical experience level, specialization, and previous courses.²¹ The purposive sampling was performed as follows; a LinkedIn call approached the first four participants. These four self-registered therapists were very consciously engaged in their development within physiotherapy. That is why it was decided, from the fifth participant onwards, to select the participants via an internet search and approaching mental health physiotherapists and manual therapists via the professional associations. We searched the internet via a google search with the words 'physiotherapist' and 'neck pain' linked to a specific land region. The participants were always selected and invited after two taken and analyzed interviews to support the purposive sampling. The inclusion criteria and analyzed interview data were used to select the new possibly deviating participants. No participants dropped out, and only two refused to participate due to the time load.

Ethical approval and consent to participate was not required based on the Medical Research Involving Human Subjects Act (WMO). Written informed consent was obtained from all participants before conducting the interviews, including their approval for using audio recording for our research.

Setting

As the COVID pandemic and associated measures prohibited personal contacts after September 2020, the data were collected both in the clinic and through the secured chat-based collaboration platform Microsoft Teams.

Data collection

Semi-structured interviews with practicing physiotherapists were conducted between June 2020 – April 2021. All interviews were audio-recorded.

The final interview guide (Table 7.1) was developed in advance by the research team. Questions were developed through a literature review, the clinical experience of the research team, and the KAP- framework. In addition, we added a vignette with clinical questions, in order to get a broad sense of the knowledge, attitude and practice behavior of the therapist. Three pilot interviews with a physiotherapist studying mental health, one physiotherapist specialist in manual therapy, and one physiotherapist-researcher were audiotaped, transcribed, and reviewed by the first author to refine the interview guide. The main change was that the physiotherapists were asked to describe two diverse cases of their patients with NP, rather than to reflect on a vignette supplied by the interviewer, to elicit a more comprehensive range of beliefs and candid opinions from personal experiences. The three pilot interviews were not included in the analysis.

Table 7.1: Final interview guide

Questions regarding the submitted cases and planned follow up questions
• Why did this patient consult you? • What do you think caused the neck pain? • To what extent did you feel that you could help this patient? • What do you think supported recovery in this patient? ◦ What role did you / or could you play in this? • What do you think was holding back this patient's recovery? ◦ What role did you / or could you play in this? • Can you tell me what the treatment looked like for this patient? ◦ Could you tell me why you choose this treatment/strategy? • What role did you play in this patient's process? • Have you encountered any obstacles in the treatment of this patient?

After the first official four interviews, the interview guide was revised through an iterative process. This revision allowed us during the following interviews to focus more on the physiotherapist's attitude and practice behavior in patients with NP. All questions that did not add relevant information to answer the research

question were removed (e.g., generic questions such as years of work experience or what kind of patients do you treat); no questions were added.

Personal characteristics interviewers

All interviews were conducted by both a researcher and one mental health physiotherapist (M.V. and N.K. or F.J.). A conscious decision was made to have two interviewers with different backgrounds conduct the interviews in order to avoid potential information bias.²² The lead interviewer (M.V.) is a manual therapist with 13 years of work experience in private practice and a clinical and research interest in NP prognostic factors. In addition, this interviewer followed various qualitative research courses with practical exercises in interviewing and data analysis and taught qualitative research methodology and data analysis in physiotherapy master courses. N.K. and F.J. are mental health physiotherapists and were present to observe and ask additional questions. They observed potential discrepancies between non-verbal signs and verbal statements and responded if necessary. In addition, they asked in-depth questions about more mental health-related statements from the participants.

Theoretical framework

The ‘KAP-framework’ was used as a sensitizing concept (Figure 7.1).²³ This concept was the starting point for our data analysis and functioned as an analytic lens throughout the process.²⁴ However, this sensitizing concept was not forced on the data, facilitating the possibility of an inductive analysis.²⁴ Qualitative content analysis with an inductive approach was used to analyze the data.²⁵

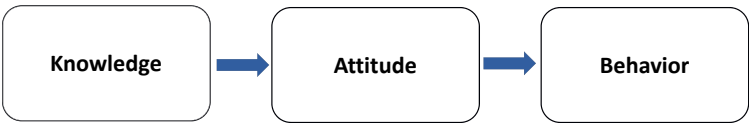


Figure 7.1: Sensitizing concept ‘Knowledge, attitude and practice framework’²³

Data analysis

All interviews were transcribed verbatim by final-year physiotherapy students using Amberscript as support. Amberscript is a website that automatically transforms audio into text using speech recognition (www.amberscript.com).

The first author checked each transcribed interview for accuracy and sent the transcript to the participant for potential comment.

After the first official interview, all coders (M.V., N.K., and F.J.) open-coded the text line by line, following a group meeting to discuss and define the open codes. Subsequently, all interviews were independently open-coded by M.V. and N.K. or F.J. following a consensus meeting. Every second interview was compared by the first author with the previous analysis to identify similarities and differences and discussed with the other two coders. In addition, the data were also triangulated during the analytical process by a continued dialogue between the coders to clarify insights where there were disagreements or alternative explanations.

Codes were arranged into categories, evaluated by abstraction, and further reduced to generic and main categories.²⁵ These main categories are named themes in this paper. After every fourth interview, pre-planned individual regular meetings with the second and third authors (H.W. and M.G.) were held, providing the opportunity to re-examine the qualitative data with fresh pairs of eyes. Overall saturation was reached during the process when both inductive thematic and data saturation appeared. The inductive thematic saturation appears confined to the level of analysis, focuses on identifying new codes, categories, and themes, and was based on the number of codes. The data saturation was a matter of identifying redundancy in the data; saturation appears distinct from the formal data analysis. Thematic and data saturation appeared when no new data was gathered from participants and added to our model.²⁶

The computer software Atlas.ti was used to facilitate the data analysis process.²⁷

Member checking was carried out to validate themes and categories by sending a video presentation of the results. During the presentation, themes and categories could be read verbatim. A spoken explanation was chosen to clarify the relationship that has been established the mutual relationships and could therefore be reviewed better than by a written check alone. The participants were provided the opportunity to respond by email within 2 weeks to the findings and affirm the accuracy and completeness of the results.

Results

Thirteen interviews were held with physiotherapists working in primary physiotherapy care across the Netherlands. Interviews lasted between 43 and 90 minutes (mean = 62 min, SD = 13 min). Thematic saturation occurred after the 13th interview; as the data of this last interview did not lead to any new emergent themes.^{26,28} Seven males and 6 females, median age 39 (range 25–65) years, participated in the study. All physiotherapists had a bachelor's degree in physiotherapy and participated in different postgraduate courses or were specialists in manual therapy (46%), mental health (39%), or human movement sciences (8%) with a master's degree.

Sample

The demographic and educational characteristics of the participants are summarized in Table 7.2.

Findings

As presented in Table 7.3, seven themes, 16 categories, and six subcategories emerged from the qualitative analysis resulting in an adjusted knowledge, attitude, and practice model (Figure 7.2). This model shows how the various findings are related to each other. Quotes from the participants are used to illuminate the findings.

With regard to the member-checking process, all 13 physiotherapists were invited to provide feedback on a video report of the findings. The four participants who responded, indicated that they were in agreement with the findings.

Theme 1: Physiotherapists self-estimated knowledge and attitude

While describing the physiotherapists' individual clinical cases, all physiotherapists mentioned that in general they think that psychosocial factors influence their patients' (non)recovery or pain experience during their treatment process. They often implied that stress from work or personal situations (e.g., children or a hectic social life) contributes to the development and non-recovery of NP. The psychological factors 'fear of movement' and 'anxiety', were most frequently mentioned as negative factors for recovery when describing the treatment process. While ten physiotherapists specifically described the relationships between biomedical and

Table 7.2: Demographic and educational characteristics of participants

Participant	Gender	Age	Experience in years	Qualification and specialization	Postgraduate courses	Number of NP patients per week
1	Male	25–30	4	BPT, MPT Manual Therapy	Dry needling Pain Sciences Practical manual therapy techniques	> 5 patients per week
2	Female	25–30	3	BPT, MPT Mental health	None	> 5 patients per week
3	Male	35–40	14	BPT, MPT Manual Therapy	(Sport) Rehabilitation	> 5 patients per week
4	Male	35–40	13	BPT, MPT Manual Therapy	Pain Sciences Practical manual therapy techniques	> 5 patients per week
5	Male	60–65	40	BPT, MPT Manual Therapy	Communication Dry needling Practical manual therapy techniques	> 5 patients per week
6	Female	50–55	32	BPT, MPT Mental health	Behavioral therapy Mental Health Practical manual therapy techniques	> 5 patients per week
7	Male	60–65	34	BPT, MPT Manual Therapy	Practical manual therapy techniques (Sport) Rehabilitation	> 5 patients per week
8	Male	30–35	5	BPT	Central disorders (Sport) Rehabilitation	1 to 5 patients per week
9	Female	60–65	36	BPT, MPT Mental health	Alternative Medicine Mental Health Practical manual therapy techniques	1 to 5 patients per week
10	Female	45–50	15	BPT, MPT Human Movement Sciences	Central disorders Communication (Sport) Rehabilitation	< 5 patients per week
11	Female	45–50	25	BPT, MPT Mental health	Communication Mental Health Practical manual therapy techniques	> 5 patients per week
12	Male	35–40	16	BPT, MPT Mental health	Behavioral therapy Coaching Taping	> 5 patients per week
13	Female	25–30	4	BPT, MPT Manual Therapy	None	1 to 5 patients per week

Abbreviations; BPT = Bachelors of Physiotherapy, MPT = Masters of Physiotherapy, Postgraduate course categories: Communication, Taping, Dry needling, Coaching, Mental Health, Pain Science, Alternative Medicine mental health, (Sport) Rehabilitation, Behavioral therapy, Practical manual therapy techniques, Central disorders.

Table 7.3: Themes, categories and subcategories

Theme	Category	Subcategory
1. Physiotherapists self-estimated knowledge and attitude	Nonspecific neck pain can have an underlying mechanical and/or psychosocial factor Potential prognostic factors are mostly of a psychosocial character Awareness and importance for a 'broad view' on the patient	
2. Role clarity	Role boundaries differ regardless of specialization or age A physiotherapist has to be coach, advisor, providing insight into the NP complaints and has the role to comfort the patient	
3. Therapeutic relationship	Therapeutic alliance is an important aspect of the therapeutic process Responsibility for recovery rests with the patient	Going along with patient expectations and hands-on treatment can support alliance
4. Internal barriers practice behavior	Basic knowledge and skills Routines and habits Feeling of impotence to modify patients' external factors	
5. External barriers practice behavior	Patients are not interested in a broader approach	
6. Physiotherapists' practice behaviors	Experience based assessment rather than structured assessment on (prognostic) psychosocial factors Experience based support as interventions rather than structured interventions on (prognostic) psychosocial factors Physical approach for assessment and treatment Tendency to go along with patient expectations	Minimal use of questionnaires by physiotherapists and manual therapists Minimal use of guidelines Physical approach with objectives on several dimensions within the bio-psychosocial domain Tendency 'to feel' whether there is an opening for a psychosocial approach under mental health physiotherapists
7. Self-reflection	Confidence in knowledge and skills among physiotherapists increases with work experience	Learning by doing and experience- based practice

psychosocial factors as the cause of their NP cases, the other three physiotherapists described a purely biomedical cause. These therapists all specialized in manual therapy.

Most of the participating physiotherapists reported that they started their career holding a very biomedical perspective. Due to work experience however, their attitude did change to a more biopsychosocial approach. Only the three youngest physiotherapists reported that their post-bachelor education had a role in their change toward a more biopsychosocial attitude. One physiotherapist described:

“I was convinced that as a manual therapist, you are the only person who can help a patient with NP. And fortunately, I am now thirteen years further, and I have taken those blinders off and started to look wider. A broader look is needed at neck complaints than just looking purely somatically, segments that are stuck, or muscles that are hyper-tonic. That is much less of a concern to me. So, I’m actually a lot more concerned about the person I have actually in front of me.” (Physiotherapist 4)

Theme 2: Role clarity

The majority of the physiotherapists described a broadening of their treatment roles over the years. Manual therapists in particular experienced expanding into the psychosocial domain, whereas the biomedical domain was their sole standard in their first working years. Some described long waiting lists to psychologists led them to trying to address the psychosocial aspects themselves, which added to their knowledge and experience in the ensuing patients. Although almost all therapists experience this role broadening, there are differences in their role boundaries when treating psychosocial aspects in patients with NP. Two therapists mentioned that they did not have any boundaries when assessing or treating psychosocial aspects (e.g., depression, burn-out, stress). Almost half of the physiotherapists were uncertain whether their role should include treating those aspects, and four were very clear that the problem must always be approachable from the physical aspect. These different role boundaries were, in the studied group, independent of specialization or age. Nearly all physiotherapists considered that coaching, advising, and providing insight into the NP complaints were the most important roles they had to play during the therapeutic process.

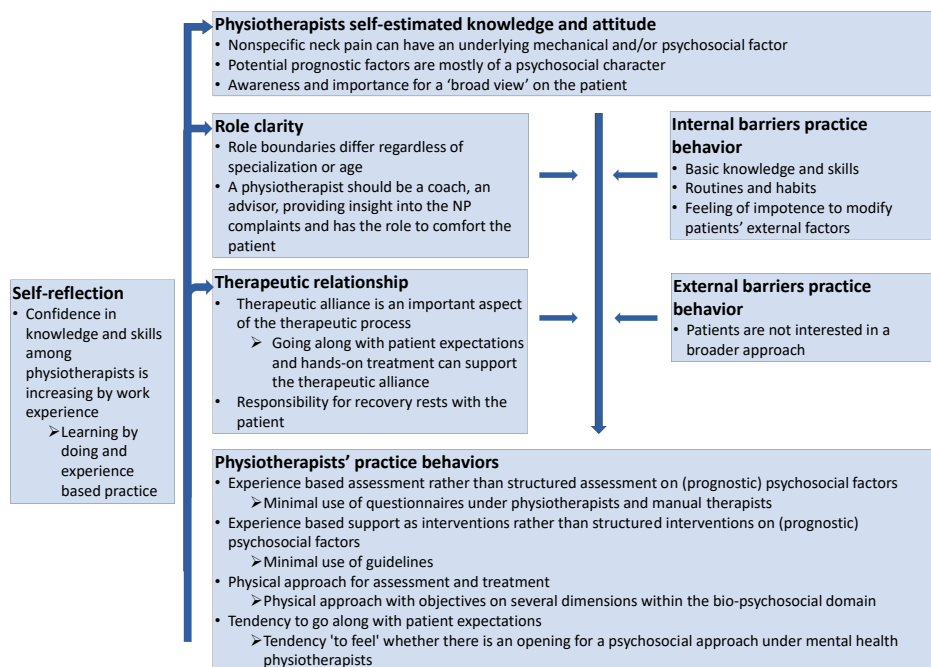


Figure 7.2: Themes, categories and subcategories in an adjusted knowledge, attitude and practice model.

Theme 3: Therapeutic relationship

The two most frequently mentioned codes within this theme were cooperation and trust. According to the participating physiotherapists, trust between the therapist and patient plays an essential role in how patients cooperate to achieve goals in their recovery.

Most physiotherapists in this study reported that going along with patients is a considered choice that can support the therapeutic alliance, where the therapeutic alliance is described as the positive connection and working relationship between the therapist and the patient.

One physiotherapist described this as follows:

“What I sometimes do, in the beginning, I also want to gain confidence when a patient asks a lot. ‘You are going to help me with that’... and it goes against my principles; often, I do what they ask of me to gain confidence.” (Physiotherapist 1)

In addition, hands-on approaches were often used to support the alliance between the therapist and the patient.

Almost all physiotherapists in this study shared a similar opinion on dependency and responsibility for recovery:

“You really want to avoid dependency.” (Physiotherapist 3)

*“She must understand that she must do something to help herself.”
(Physiotherapist 12)*

Only one physiotherapist said that he accepted that some patients just came for his physical treatment and did nothing by themselves to recover or prevent the next NP episode.

Theme 4: Internal barrier practice behavior

Some physiotherapists argued that their knowledge about psychosocial factors and skills in assessing and/or treating them are only basic and considered themselves inadequate to deal with more complex psychosocial factors (e.g., depression, anxiety, and catastrophizing). The most frequently mentioned skill to approach these psychosocial factors was adequate verbal and non-verbal communication. Although several therapists reported that they have developed communication skills over the years, some physiotherapists still questioned their own competence. Two physiotherapist described this as:

“Those prognostic factors, I think we are very well able to identify them, but not always able to deal with them.” (Physiotherapist 13)

“After signaling psychosocial prognostic factors, I try to put the neck complaints in perspective. Then I try to adjust my communication techniques accordingly. And I have to say, maybe that would be nice, to have some basis in that, to have certainty in that to be more competent... conscious ability instead of getting it done unconsciously.” (Physiotherapist 3)

The majority of the physiotherapists who implied that patients' external factors such as work or personal situations contribute to the development and non-recovery of NP found it challenging to deal with these factors in the treatment process. Although they know this can be important, they did not expect that they could influence it. One physiotherapist described this as:

“Some patients just have a job and have children, then it is often just busy. You notice that these are factors that you cannot really change; those children and that work is there. How are you going to influence that? And you don’t want to keep treating this patient forever. Those are the cases where I find it difficult.” (Physiotherapist 1)

Although most physical therapists described that a broad view of assessing and treating a patient with NP is essential, some manual therapists found it challenging to always accomplish this and therefore reverted to their routines and habits, falling back on their somatic approach.

In addition, some physiotherapists indicated that to think and act from one perspective, it is also something that happens automatically. This can be the somatic as well as the psycho-social perspective. For example, one physiotherapist described is as:

“I think that we as physiotherapists play a major role in the identification and that it is also a pitfall for me, for every therapist, to quickly go in one direction and not first outline the bigger picture.” (Physiotherapist 2)

Theme 5: External barriers practice behavior

All physiotherapists specialized in mental health mentioned that they regularly recognized psychosocial factors that influence patients’ pain and (non)recovery. However, and in their opinion unfortunately, patients were not always open to address these factors during a treatment process. The physiotherapists described this as:

“Which, on the one hand, is sometimes a bit of a shame, isn’t it, because I would like to do a little more with him in the part of self-reflection and stress reduction and the catastrophic part, to make him a bit more resilient for the future. But yes, at the moment, I can hardly attract him to my practice.” (Physiotherapist 6)

The physiotherapists described that patients become more interested in a broader approach when they experience chronic NP. In an acute or sub-acute phase of NP, patients are mostly looking for a quick fix.

Theme 6: Physiotherapists' practice behaviors

Nearly all physiotherapists described an experience-based way of assessing psychosocial factors during their history taking. This experience-based assessment characterizes itself by intuitive examining for psychosocial factors based on a gut feeling, careful attention to non-verbal signals, follow-up questioning, an open attitude and engaging in the conversation with a patient. Only one therapist described the use of the Somatic, Cognition, Emotion, Behavior and Social method to support her broad view.²⁹

Only the physiotherapists who specialized in mental health mentioned using additional psychosocial questionnaires in their clinical decision-making. The other physiotherapists and manual therapists did not feel confident to use – or questioned the usability of these questionnaires. The following quotes indicate the reasons for this:

“I think that if you use a questionnaire, you should be able to interpret it. And you also have to do something with it... and that, I often find that very difficult.” (Physiotherapist 7)

“We always take standard questionnaires. But, I have to say that I do not attach great value to them because I think that there are some questions that I personally believe that people do not always understand completely or sufficiently understand answers... I think that I mainly get my information through the history taking.” (Physiotherapist 13)

The majority of the physiotherapists were clear about treating somatic factors (e.g., segmental mobility limitations) in how often, how long, or what outcomes they expect from their treatment. In contrast, there was an unclearness and sometimes uncertainty regarding how to treat psychosocial factors. Treatment strategies were described as “*based on feeling*” and “*estimate per treatment*.”

Almost none of the physiotherapists mentioned to use the Dutch Physiotherapy Guideline for patients with NP in their clinical decision-making. Some physiotherapists were not aware of the content, and some described that their patients did not fit in, and others indicated that the guideline did not add to their basic knowledge and experience. For example, one physiotherapist said:

“I am also a bit against it. Let me put it this way, I can't get away with it properly. I don't have the clients who fit in.” (Physiotherapist 9)

While describing the assessment and treatment choices, the majority described a physical approach, including human touch. The description of their assessment and/or treatment was often in the biomedical domain (e.g., segmental mobility assessment, mobilization, or muscle strength training); even though their objective of treatment often was directed a more psychosocial domain/factor. For example; mobility assessment or mobilization of the neck was used with the objective to reduce anxiety or fear of movement. In addition, the objective of muscle strength training or exercises was often described as allowing the patient to experience his, for example very high muscle tension or that the patient is capable of doing more than he/she thinks. Two physiotherapists described this as:

“Physical assessment of his neck and indicate that I found some increase in muscle tension in particular and that the movements left and right was equal. Well, that actually gave a lot of comfort, and you saw that his fear decreased.” (Physiotherapist 6)

“It would be best if I could just give him a bit more, in his opinion, difficult exercises. And can convince him that his body, his neck, his back can actually handle a lot more than he actually thinks.” (Physiotherapist 8)

Going along with patients' expectations of a physical treatment approach often concerned only the first period of the treatment process before eventually arriving at a treatment strategy that may be more appropriate for combating recurrence or chronification. However, in acute NP, the complaints have often already decreased to the extent that patients do not always want to pay more attention to a broader approach.

Physiotherapists specialized in mental health regularly indicated that they ‘*wait and feel*’ if there is an opening to assess or treat psychosocial factors.

Theme 7: Self-reflection

The physiotherapists who completed postgraduate courses or training in manual therapy all indicated that manual therapy specific knowledge and skills are essential for assessing and treating patients with NP. This basis gave them the confidence to rule out underlying pathology or somatic factors as a cause of NP (e.g., radiculopathy, segmental or motor control limitations). However, they described that work and life experience resulted in the way they currently treat patients, namely,

using a broader perspective. The knowledge and skills to feel confident in working from a broader perspective are not something they learned in courses, but by experimenting, experience, and just doing.

One physiotherapist described her knowledge and skills as follows:

"I always think... what works that works and then after a while, a theory has to be added. That is my approach." (Physiotherapist 11)

Discussion

Main findings

The purpose of this study was to explore physiotherapists' knowledge, attitude, and practice behavior in assessing and managing patients with non-specific, non-traumatic, acute and subacute NP with a specific focus on how they identify and modify prognostic factors for chronification. In this study, the physiotherapists had an overall biopsychosocial knowledge and attitude regarding patients with non-specific NP. While there was overlap in knowledge about the cause and prognostic factors of chronification of NP, diverse assessment and treatment strategies were reported. These strategies were mainly from a physical approach, with a tendency to go along with patients' expectations, and psychosocial assessment and treatment on prognostic factors were mostly experienced based. Physiotherapists' practice behaviors were influenced by individual attitudes towards their professional role and therapeutic relationship with the patient. Furthermore, individual knowledge and skills, personal routines and habits, the feeling of powerlessness to modify patients' external factors, and patients' lack of willingness to a biopsychosocial approach influenced physiotherapists' clinical decisions. In addition, almost all physiotherapists pointed out that self-reflection was essential for their personal development as a practitioner and that they develop themselves primarily through 'learning by doing'.

Reflection on main findings

That patients' treatment expectations and the physiotherapists' desire to maintain a healthy therapeutic relationship have previously been shown to be factors in the choice of practice behavior in low back pain.³⁰ The feeling of tension in the therapeutic relationship was also identified in other qualitative studies.^{30,31} The experiences of physiotherapists treating patients with non-specific low back pain

include conflict among their pain beliefs, attitudes, and working partnerships with patients, and treatment decisions may be influenced when physical therapists modify their beliefs and attitudes to reduce this sense of conflict and interfere with the adoption of evidence based care.^{17,32} It can be questioned if going along with patients' expectations is always the best choice, especially when this ensures that psychosocial prognostic factors are not included in the treatment process. It is reported that discrepancies in the explanation of factors involved in pain between professionals and patients were deemed to be disadvantageous to interaction and treatment outcomes.³² This strategy could lead to sufficient treatment results in the short term, but possibly cause adverse effects on the chronification of pain and patient therapeutic dependency.

Although all physiotherapists refer to communication as one of the essential skills in their treatment of patients with NP, most manual therapists particularly took somatically oriented post-graduate courses (e.g., manual therapy techniques). As they mentioned internal barriers of practice behavior, such as 'basic knowledge and skills and 'the feeling of impotence to modify patient's external factors', it seems more appropriate to take targeted communication courses to reduce these barriers effectively.³³ The finding that physical therapists reported struggles to find strategies to integrate the clinical explanation within a broader biopsychosocial framework that made sense to patients is reported earlier,¹⁸ and that training and expertise in interaction skills are important is also in line with the literature.^{33,34} Although some potential prognostic factors are mentioned in the physiotherapists' Dutch Guideline for NP, it does not give explicit instructions on how to assess these in daily practice (e.g., "collecting additional information by asking about the presence of prognostic factors").^{15,31} In addition, optional questionnaires focusing on psychosocial factors such as fear-avoidance beliefs, kinesiophobia, anxiety, depression, stress, and somatization are recommended if there is reason to do so in the history taking. Besides, the guideline not only states that the focus should be and remain during treatment on psychosocial factors through communication, less attention should be paid to pain, and more to exercise and that physiotherapists also have to evaluate whether these psychosocial factors change. Our study showed that the assessment and treatment of psychosocial factors are often done in an unstructured way. In addition, some therapists experience deficiency in selecting the appropriate questionnaires, interpreting the scores and finally carrying out the targeted therapy.

Furthermore, the Dutch guideline rightly advises that if psychosocial prognostic factors hinder recovery, it must be determined whether the physiotherapist is the most appropriate professional to target these factors or to advise the patient to contact another more appropriately skilled professional. However, given the different attitudes towards the role and role boundaries of the physiotherapists, it is highly questionable whether this is done accordingly. Not following recommended treatments in evidence-based guidelines when managing musculoskeletal conditions and a difference in the state of science and clinical practice concerning prognostic factors has been reported previously.^{31,32} It seems advisable for guidelines to provide more substance to their recommendations. For instance, the Pain – Somatic – Cognitive – Emotional – Behavioral – Social – Motivation – model (PSCESM-model) during the intake supports a biopsychosocial approach and communication strategies seem to facilitate the coaching and advisory role (e.g., motivational interviewing or pain neuroscience education).^{29,35}

Strengths and limitations methodology

Several methodological choices have been made to accomplish credibility and dependability.

First of all, this study explored knowledge, attitude, and practice behavior and their potential interaction. We provided a confidential context for our physiotherapists by using personal cases. Through this, we attempted to explore physiotherapists' attitudes as reliable and closely as possible to their actual practice, instead of measuring the explicit attitude with the commonly used Pain Attitudes and beliefs Scale for physiotherapists,^{36,37} which is open to social-desirability bias. In addition, we experienced limitations in our pilot interviews when using a vignette, even though a vignette has previously been shown to have acceptable validity.^{38,39} The physiotherapists' descriptions of their own patients gave us in-depth information about their attitude and practice behavior. However, to further reduce potential bias in exploring physiotherapists' implicit attitude, a practice observational study should be done.

Secondly, to prevent the risk of potential bias in data collection, all interviews were conducted by two researchers with both mental health and manual physiotherapy background, and all with many years of clinical experience in working with patients with acute NP. Familiarity with the context can be a valuable asset to collect, interpret and analyze data, facilitating face validity.⁴⁰

Thirdly, the analytical rigor was strengthened by data and investigator triangulation by: (1) interviewing multiple participants, (2) independently coding the transcripts by two coders, (3) continued dialog between the coders, and (4) the regular meetings with the second and third author to re-examine the qualitative data. In addition, the results of the analysis were checked by the participants and approved by four participants.

Fourth, there was a fair distribution of male and female participants, a broad range in age, and various physiotherapy treatment specializations, allowing to present a general picture of physiotherapists in the Netherlands. However, 92% of the physiotherapists had a master's degree; it can be questioned whether these findings also apply to physiotherapists holding a bachelor's degree. Fifth, the quality of the interview data allowed us to provide detailed descriptions and quotations throughout the article, which strengthened the credibility of the findings.

In addition, we attempted transferability by accurately describing the context, characteristics of participants, data collection, and data analysis process. However, the findings of data provided by physiotherapists working in Dutch primary care practice might not be transferable to other countries and settings.

In qualitative research, there is no commonly used method to calculate the sample size. As advised, our sample size was based on a combination of careful stratification, information power and achieving saturation.^{41,42} Information power indicated that the more information the sample holds relevant to the actual study, the lower the number of participants is needed.⁴¹ Based on information power, our sample size is likely sufficient; the primary substantiation is the quality of our in-depth interviews and the narrowness of our study aim. Concerning saturation, theme saturation occurred after 13 interviews.

Clinical message and future directions

This study highlights the importance of factors other than knowledge in physiotherapists' practice behavior. Physiotherapists seem to know the biopsychosocial character of non-specific, acute and subacute NP. However, the translation from knowledge to practice behavior involves more factors that need to be addressed to develop knowledge-based coherent practice behavior. In particular, the physiotherapist's self-reflective ability can help the physiotherapist to continue developing and applying behavioral change within his practice behavior. The self-reflective ability must be an essential point of attention in physiotherapy education, and

professional associations should concentrate on self-reflection in the form of peer review, aimed at optimizing attitude and practice behavior.

In addition, further research must be done on reducing the internal and external barriers effectively, with the main aim that the biopsychosocial model, for which the knowledge already appears to be present, is standardly applied within both assessment and treatment in patients with non-specific NP.

Conclusion

This is the first study to explore the knowledge, attitude, and practice behavior of physiotherapists regarding non-specific acute and subacute NP and potential modifiable prognostic factors. We found a greater understanding of the non-coherent relation between knowledge, attitude, and practice behavior in the biopsychosocial approach and potential barriers connecting these domains in patients with non-specific NP.

References

1. GBD 2015 Disease and Injury Incidence and Prevalence Collaborators. Global, regional, and national incidence, prevalence, and years lived with disability for 310 diseases and injuries, 1990–2015: a systematic analysis for the Global Burden of Disease Study 2015. *Lancet* (London, England). 2016;388:1545–602. doi:10.1016/S0140-6736(16)31678-6.
2. Hoy D, Geere J-A, Davatchi F, Meggitt B, Barrero LH. A time for action: Opportunities for preventing the growing burden and disability from musculoskeletal conditions in low- and middle-income countries. *Best Pract Res Clin Rheumatol*. 2014;28:377–93. doi:10.1016/j.berh.2014.07.006.
3. Hurwitz EL, Randhawa K, Yu H, Côté P, Haldeman S. The Global Spine Care Initiative: a summary of the global burden of low back and neck pain studies. *Eur Spine J*. 2018;27:796–801. doi:10.1007/s00586-017-5432-9.
4. Childs JD, Cleland JA, Elliott JM, Teyhen DS, Wainner RS, Whitman JM, et al. Neck Pain: Clinical practice guidelines linked to the international classification of functioning, disability, and health from the orthopedic section of the american physical therapy association. *J Orthop Sport Phys Ther*. 2008;38:A1–34. doi:10.2519/jospt.2008.0303.
5. Côté P, Cassidy DJ, Carroll LJ, Kristman V. The annual incidence and course of neck pain in the general population: a population-based cohort study. *Pain*. 2004;112:267–73. doi:10.1016/j.pain.2004.09.004.
6. Croft PR, Lewis M, Papageorgiou AC, Thomas E, Jayson MI, Macfarlane GJ, et al. Risk factors for neck pain: a longitudinal study in the general population. *Pain*. 2001;93:317–25. <http://www.ncbi.nlm.nih.gov/pubmed/11514090>. Accessed 14 Feb 2018.
7. van den Dool J. NIVEL Zorgregistraties eerste lijn - Zorg door de fysiotherapeut jaarcijfers 2016 en trendcijfers 2011–2016. 2016. https://www.nivel.nl/sites/default/files/bestanden/2016_jaarrapport_fysiotherapie.pdf. Accessed 15 Feb 2018.
8. Bovim G, Schrader H, Sand T. Neck pain in the general population. *Spine* (Phila Pa 1976). 1994;19:1307–9. doi:10.1097/00007632-199406000-00001.
9. Reid KJ, Harker J, Bala MM, Truyers C, Kellen E, Bekkering GE, et al. Epidemiology of chronic non-cancer pain in Europe: narrative review of prevalence, pain treatments and pain impact. *Curr Med Res Opin*. 2011;27:449–62. doi:10.1185/03007995.2010.545813.
10. Geneen LJ SB, Andrew Moore R, Clarke C, Martin D, Colvin LA, Smith BH. Cochrane Database of Systematic Reviews Physical activity and exercise for chronic pain in adults: an overview of Cochrane Reviews (Review) Physical activity and exercise for chronic pain in adults: an overview of Cochrane Reviews (Review) i Physical acti. *Cochrane Database Syst Rev*. 2017. doi:10.1002/14651858.CD011279.pub3.
11. Bertozzi L, Gardenghi I, Turoni F, Villafañe JH, Capra F, Guccione AA, et al. Effect of Therapeutic Exercise on Pain and Disability in the Management of Chronic Nonspecific Neck Pain: Systematic Review and Meta-Analysis of Randomized Trials. *Phys Ther*. 2013;93:1026. Accessed 14 Feb 2018.
12. Gross A, Langevin P, Burnie SJ, Bédard-Brochu M-S, Empey B, Dugas E, et al. Manipulation and mobilisation for neck pain contrasted against an inactive control or another active treatment. *Cochrane Database Syst Rev*. 2015;23. doi:10.1002/14651858.CD004249.pub4.
13. Swinkels J, van der Feltz-Cornelis CM (Eds.). *Multidisciplinaire richtlijn SOLK en somatoforme stoornissen*. Utrecht: Trimboos-instituut; 2010.

14. Verwoerd M, Wittink H, Maissan F, Smeets R. Consensus of potential modifiable prognostic factors for persistent pain after a first episode of nonspecific idiopathic, non-traumatic neck pain: results of nominal group and Delphi technique approach. *BMC Musculoskelet Disord.* 2020;21:656. doi:10.1186/s12891-020-03682-8.
15. Bier JD, Scholten-Peeters GGM, Staal JB, Pool J, van Tulder M, Beekman E, Meerhoff GM, Knoop J, Verhagen AP. KNGF-richtlijn Nekpijn - praktijkrichtlijn. 2016.
16. Alexanders J, Anderson A, Henderson S. Musculoskeletal physiotherapists' use of psychological interventions: A systematic review of therapists' perceptions and practice. *Physiother (United Kingdom).* 2015;101:95–102.
17. Jeffrey JE, Foster NE. A Qualitative Investigation of Physical Therapists' Experiences and Feelings of Managing Patients With Nonspecific Low Back Pain. *Phys Ther.* 2012;92:266–78.
18. Sanders T, Foster NE, Bishop A, Ong BN. Biopsychosocial care and the physiotherapy encounter: Physiotherapists' accounts of back pain consultations. *BMC Musculoskelet Disord.* 2013;14.
19. Ajzen I. Nature and Operation of Attitudes. *Annu Rev Psychol.* 2001;52:27–58. doi:10.1146/annurev.psych.52.1.27.
20. Tong A, Sainsbury P, Craig J. Consolidated criteria for reporting qualitative research (COREQ): a 32-item checklist for interviews and focus groups. *Int J Qual Heal Care.* 2007;19:349–57. doi:10.1093/intqhc/mzm042.
21. Parsons M, Greenwood J. A guide to the use of focus groups in health care research: Part 1. *Contemporary nurse : a journal for the Australian nursing profession.* 2000;9:169–80.
22. Chenail RJ. Interviewing the investigator: Strategies for addressing instrumentation and researcher bias concerns in qualitative research. *Qual Rep.* 2011;16:255–62.
23. Alzghoul BI, Chew Abdullah NA. Psychosocial Theories and Pain Management Practices: A Review of Empirical Research. *Mediterr J Soc Sci.* 2015;6:60–7.
24. Bowen GA. Grounded Theory and Sensitizing Concepts. *Int J Qual Methods.* 2006;5:12–23.
25. Elo S, Kyngäs H. The qualitative content analysis process. *J Adv Nurs.* 2008;62:107–15. doi:10.1111/j.1365-2648.2007.04569.x.
26. Saunders B, Sim J, Kingstone T, Baker S, Waterfield J, Bartlam B, et al. Saturation in qualitative research: exploring its conceptualization and operationalization. *Qual Quant.* 2018;52:1893–907. doi:10.1007/s11135-017-0574-8.
27. T. M. Atlas.ti Scientific Software Development GmbH. 2006.
28. Olshansky EF. Generating Theory Using Grounded Theory Methodology. In: Chesnay M de, editor. *Nursing research using grounded theory Qualitative designs and methods.* New York: Springer; 2015. p. 19–28.
29. Wijma AJ, van Wilgen P, Meeus M, Nijs J. Clinical biopsychosocial physiotherapy assessment of patients with chronic pain: The first step in pain neuroscience education. *Physiother Theory Pract.* 2016;32:368–84.
30. Corbett M, Foster N, Ong BN. GP attitudes and self-reported behaviour in primary care consultations for low back pain. *Fam Pract.* 2009;26:359–64.
31. Dahan R, Borkan J, Brown JB, Reis S, Hermoni D, Harris S. The challenge of using the low back pain guidelines: A qualitative research. *J Eval Clin Pract.* 2007;13:616–20.

32. O'Keeffe M, Cullinane P, Hurley J, Leahy I, Bunzli S, O'Sullivan PB, et al. What influences patient-therapist interactions in musculoskeletal physical therapy? Qualitative systematic review and meta-synthesis. *Phys Ther.* 2016;96:609–22.
33. Holopainen R, Vuoskoski P, Piirainen A, Karppinen J, O'sullivan P. Patients' conceptions of undergoing physiotherapy for persistent low back pain delivered in Finnish primary healthcare by physiotherapists who had participated in brief training in cognitive functional therapy. *Disabil Rehabil.* 2022;44:3388–99.
34. Dukhu S, Purcell C, Bulley C. Person-centred care in the physiotherapeutic management of long-term conditions: a critical review of components, barriers and facilitators. *Int Pract Dev J.* 2018;8:1–27
35. Nijs J, Wijma AJ, Willaert W, Huysmans E, Mintken P, Smeets R, Goossens M, van Wilgen CP, Van Bogaert W, Louw A, Cleland J, Donaldson M. Integrating Motivational Interviewing in Pain Neuroscience Education for People With Chronic Pain: A Practical Guide for Clinicians. *Phy Ther.* 2020;100:846–59.
36. Mutsaers J-HAM, Pool-Goudzwaard AL, Ostelo RWJG, Peters R, Koes BW, Verhagen AP. The psychometric properties of the PABS-PT in neck pain patients: A validation study. *Man Ther.* 2014;19:208–14. doi:10.1016/j.math.2013.12.004.
37. Ostelo RWJ, Stomp-van den Berg SG, Vlaeyen JW, Wolters PMJ, de Vet HC. Health care provider's attitudes and beliefs towards chronic low back pain: the development of a questionnaire. *Man Ther.* 2003;8:214–22. doi:10.1016/S1356-689X(03)00013-4.
38. Peabody JW, Luck J, Glassman P, Dresselhaus TR, Lee M. Comparison of Vignettes, Standardized Patients, and Chart Abstraction. *JAMA.* 2000;283:1715. doi:10.1001/jama.283.13.1715.
39. Rutten GMJ, Harting J, Rutten STJ, Bekkering GE, Kremers SPJ. Measuring physiotherapists' guideline adherence by means of clinical vignettes: a validation study. *J Eval Clin Pract.* 2006;12:491–500. doi:10.1111/j.1365-2753.2006.00699.x.
40. Krippendorff K. *Content Analysis An introduction to Its Methodology.* SAGE; 2013.
41. Malterud K, Siersma VD, Guassora AD. Sample Size in Qualitative Interview Studies. *Qual Health Res.* 2016;26:1753–60. doi:10.1177/1049732315617444.
42. Morse JM. The significance of saturation. *Qual Health Res.* 1995;5:147–9.

Appendix 7.1: COREQ 32- item Checklist for Qualitative studies

No. item	Guide question / description	
Domain 1: Research team and reflexivity		
Personal characteristics		
1. Interviewer / facilitator	Which author/s conducted the interview or focus group?	First author (M.V.) and two mental health physiotherapy students N.K. and F.J.
2. Credentials	What were the researcher's credentials?	Msc (M.V.) and Msc third year students (N.K. and F.J.) and physiotherapists.
3. Occupation	What was their occupation at the time of the study?	Phd student and lecturer Msc manual therapy (M.V.) Msc third year students mental health and working in physiotherapy practice (N.K. and F.J.).
4. Gender	Was the researcher male or female?	Females
5. Experience and training	What experience or training did the researcher have?	Qualitative research courses with practical exercise in interviewing and data analysis. Teaching qualitative research methodology and data analysis in physiotherapy master courses. Specific for this study; three pilot interviews with observation of experienced interviewers.
Relationship with participants		
6. Relationship established	Was a relationship established prior to study commencement?	The participants had only contact by email before the interviews.
7. Participant knowledge of the interviewer	What did the participants know about the researcher? e.g. personal goals, reasons for doing the research?	Only two participants (number 1 and 2) knew the researcher from earlier physiotherapy courses. An introduction email was sent with information about the research question, and the participants were asked to think about two cases that we would discuss during the interview.

Appendix 7.1 continues on next page.

Appendix 7.1: Continued

No. item	Guide question / description	
8. Interviewer characteristics	What characteristics were reported about the interviewer/ facilitator? e.g. Bias, assumptions, reasons and interests in the research topic.	All interviews were conducted by a researcher and a mental health physiotherapist. The lead interviewer was a female manual therapist with 13 years of work experience in private practice and a clinical and research interest in neck pain prognostic factors. N.K. and F.J. were mental health physiotherapists (N.K. and F.J.) and were present to observe and added questions. N.K. had F.J. both had eight years of work experience in private practice.
Domain 2: Study design		
Theoretical framework		
9. Methodological orientation and Theory	What methodological orientation was started to underpin the study? E.g. grounded theory, discourse analysis, ethnography, phenomenology, content analysis	Qualitative content analysis.
Participant selection		
10. Sampling	How were participants selected? Eg. purposive, convenience, consecutive, snowball	Purposive sampling.
11. Method of approach	How were participants approached? E.g. face-to-face, telephone, mail, email	The participant were approach by email.
12. Sample size	How many participants were in the study?	13 participants
13. Non-participation	How many people refused to participate or dropped out? Reasons?	No participates dropped out. Two refused to participate due to time load.

Setting		
14. Setting of data collection	Where was the data collected? E.g. home, clinic, workplace	The data were collected in the clinic and through MStems.
15. Presence of non-participants	Was anyone else present besides the participants and researchers?	No.
16. Description of sample	What are the important characteristics of the sample? E.g. demographic data, date	Seven males and females, median age 39 (range 25 - 65) years, participated in the study. See table 1 in the results section.
Data collection		
17. Interview guide	Were questions, prompts, guides provided by the authors? Was it pilot tested?	The interview guide was developed in advance by the research team. Questions were developed through a literature review, the clinical experience of the research team, and the knowledge, attitude and behavior framework. Three pilot interviews were audiotaped, transcribed, and reviewed by the first author to refine the interview guide further.
18. Repeat interviews	Were repeat interviews carried out? If yes, how many?	No
19. Audio/visual recording	Did the research use audio or visual recording to collect the data?	Audio recording.
20. Field notes	Were field notes made during and/or after the interview or focus group?	Field notes were made by the second interviewer. Focused on non-verbal interaction.
21. Duration	What was the duration of the interviews or focus group?	Interviews lasted between 43 and 90 minutes (mean = 62 min, SD = 13 min).
22. Data saturation	Was data saturation discussed?	Yes, both with data coders and the research team.
23. Transcripts returned	Where transcripts returned to participants for comment and/or correction?	The transcripts were returned to the participants.

Appendix 7.1 continues on next page.

Appendix 7.1: *Continued*

No. item	Guide question / description	
Domain 3: Analysis and findings		
Data analysis		
24. Number of data coders	How many data coders coded the data?	There were three data coders involved. Every interview description was coded by two data coders. Only the first interview was coded by all three data coders.
25. Description of the coding tree	Did authors provide a description of the coding tree?	After the first interview, all researchers (M.V., N.K., and F.J.) open-coded the text line by line, following a group meeting to discussed and defined the open codes. Subsequently, all interviews were independently open-coded by M.V. and N.K. or F.J. following a consensus meeting. Every second interview was compared with the previous analysis to identify similarities and differences by the first author and were discussed with the other two coders.
26. Derivation of themes	Were themes identified in advance or derived from the data?	Derived from the data.
27. Software	What software, if applicable, was used to manage the data?	Atlas.ti
28. Participant checking	Did participants provide feedback on the findings?	The participants received a video presentation of the findings and had the opportunity to react.
Reporting		
29. Quotations presented	Were participant quotations presented to illustrate the themes/findings? Was each quotation identified? E.g. participant number	Yes See quotations in the text in the result section.
30. Data and findings consistent	Was there consistency between the data presented and the findings?	Yes See Table 7.3 and Figure 7.2 and text in the result section.
31. Clarity of major themes	Were major themes clearly presented in the findings?	Yes See Table 7.3 and Figure 7.2 and text in the result section.
32. Clarity of minor themes	Is there a description of diverse cases or discussion of minor themes?	Yes See text in the result section.





Chapter 8

General discussion

General discussion

In this final chapter of the thesis, the main findings of all studies are briefly summarized, and their significant implications are underscored. This is followed by a more in-depth general discussion of selected themes, methodology, and a view of future research and clinical practice, all crucial for advancing our understanding and management of non-specific, non-traumatic neck pain (NSNP).

Summary and discussion of the main findings

This dissertation undertook a structured exploration to understand NSNP and the role of physiotherapists in its assessment and management. A systematic review and a Delphi study are presented in the first part to identify and synthesize modifiable and non-modifiable prognostic factors for neck pain chronification, establishing a crucial foundation for the prognostic study. The second part describes the development and internal validation of a prognostic model for neck pain chronification, detailing the longitudinal cohort's methodological approach and outcomes while exploring the impact of pain severity on patients' functioning as defined by the ICF. The final part focuses on physiotherapists, exploring their knowledge, attitudes, and behaviors in managing NSNP.

Chapter 2 of this dissertation presents a systematic review to identify prognostic factors for the chronification of neck pain and perceived non-recovery of patients with NSNP. This review underscores the moderate evidence suggesting age over 40 and concurrent back pain as prognostic factors for the chronification of neck pain. In addition, previous neck pain episodes and concurrent headaches are moderately indicative of self-perceived non-recovery (i.e. 'completely recovered to worse than ever'), at 12 months. Despite these findings, the quality of evidence is deemed low to very low, highlighting a gap in the current understanding of prognostic factors.

Chapter 3 focuses on reaching consensus among experts regarding potential prognostic factors, particularly those modifiable by physiotherapeutic interventions, using a Modified Nominal Group Technique and a Delphi survey. This effort culminated in identifying 26 prognostic factors, 19 of which are modifiable through physiotherapy, notably including 14 psychological or behavior factors. This underscores the importance of incorporating a biopsychosocial approach in future prognostic research.

Chapter 4 and **Chapter 5** report the successful development and internal validation of a prognostic model for the chronification of NSNP in patients seeking physiotherapy, conducted from January 2020 to March 2023 across 30 primary practices. This prospective cohort study included 603 participants, of whom 10% developed chronic neck pain. Univariable analyses identified significant prognostic factors of pain chronification, including sex (female), higher baseline pain intensity, longer duration of neck pain, pain in different body regions, the onset of headache since the neck pain, higher disability scores, unemployment, higher scores on catastrophizing, illness beliefs about recovery (concerned and duration), depression, distress, and lower treatment beliefs. The final multivariable model, showing an optimism-corrected Area Under the Curve (AUC) of 0.83 and a corrected R^2 of 0.24, demonstrated excellent predictive accuracy and a good fit (Hosmer-Lemeshow test $P = 0.72$). The prognostic factors included in the multivariable model are sex (female), higher pain intensity at baseline, reported pain in different body regions, headache since the neck pain, headache(s) prior to neck pain, an inability or neutral score on self-modify posture during work, not working, lower scores pain identity and treatment beliefs, higher scores in beliefs regarding recovery (duration and concerns), and higher scores on distress and self-efficacy. These findings emphasize the importance of modifiable psychological factors in chronification of NSNP.

Chapter 6 presents a cross-sectional analysis of patient presentations at baseline and the six-week follow-up point, along with a longitudinal observation of patient outcomes over six weeks, three months, and six months. This analysis explored the differences in clinical characteristics and recovery rates between patients experiencing their first episode of NSNP and those with a recurrent episode. No clinically meaningful differences were found between these groups. Additionally, the study examined the impact of pain severity on patients' functioning, illness perceptions, psychological factors, and sleep quality between patients with mild pain (1-2 Numeric Pain Rating Scale (NPRS)) and moderate to severe pain (≥ 3 NPRS) measured at six weeks after baseline. Patients with higher pain intensity significantly and clinically meaningful experience more disability, have more concerns about recovery and report lower self-efficacy scores.

The last part (**Chapter 7**) focuses on the knowledge, attitudes, and practice behavior of physiotherapists in primary care, particularly regarding managing acute and subacute NSNP and their engagement with prognostic factors for the chronifica-

tion of pain. Despite a general shift towards a biopsychosocial approach, physiotherapists face several challenges in fully integrating this perspective into their practice. These challenges stem from internal factors, such as limited knowledge and skills, routines, and habits, feeling unable to modify patients' external factors, and some external factors, including patient reluctance towards a biopsychosocial approach. In addition, role clarity and the therapists' perception that a good therapeutic alliance is essential to the therapeutic process are indispensable factors in enhancing the integration of the biopsychosocial model into practice. The study highlights the importance of enhancing training and support for physiotherapists in adopting a biopsychosocial approach, alongside the crucial role of self-reflection in professional development and practice improvement.

Strengths, limitations, and methodological considerations

This dissertation encompasses a range of strengths and limitations discussed in the respective chapters. Nonetheless, it is worth recapitulating the most significant strengths and limitations that need to be considered when interpreting the results obtained from this dissertation and initiating further research.

An essential strength of this dissertation is its robust methodology in the development and internal validation of the prognostic model (**Chapter 5**). Potential prognostic factors were selected through a systematic review (**Chapter 2**) and an international consensus study (**Chapter 3**). The study protocol (**Chapter 4**) was published before the end of our inclusion period, ensuring transparency and precision. Analytical techniques were thoroughly described, including the handling of missing data, appropriate selection of prognostic factors, and addressing issues of model overfitting and optimism in both model performance and calibration ability. Additionally, the publication of R scripts alongside the results paper enhances transparency. Moreover, the individual data from all patients upon which the model is based are accessible through a web application.

In this dissertation, we used a distinct method to measure the outcome variable of chronic pain. This required patients to report pain of at least three or more on an NPRS pain at each of the three-time points: six weeks, three months, and six months after their initial presentation at the physiotherapist's practice. This approach deviates from the current definition of chronic pain¹ and diverges from previous prognostic studies, which typically utilize a single time point and define

persistent pain with an even lower NPRS rating of ≥ 1 (on a scale of 0–10).^{2–4} This methodological choice probably has contributed to a lower chronification rate in our study than in these studies.^{2–4} **Chapter 6** indicates that there are only for disability, concerns and self-efficacy significant and meaningful differences between patients with mild and those with moderate to severe pain measured 6 weeks after the first consultation with the physiotherapist. This prompted me to reconsider the arbitrary cutoff point, as it may have directly influenced our prognostic study outcomes. Consequently, whether this cutoff point was the most appropriate choice for our study can be questioned. **Chapter 6** also demonstrates that patients with their first episode of neck pain and patients with a new episode of neck pain in a recurrent patron do not differ in baseline characteristics, in the categories of symptoms, lifestyle, psychological, behavioral factors and patient beliefs, nor in their recovery over time. This finding justifies their inclusion in our cohort population of (sub)acute pain patients who have not yet experienced chronic pain.

Drawing on these insights, I advocate for international collaboration and consideration regarding which patients to include in prognostic studies and intervention trials. Patients with recurrent pain and those with (sub)acute pain exhibit no baseline differences in disability and psychological factors, which generally score very low. In contrast, patients with chronic pain demonstrate higher scores on both disability and psychological factors and can thus be considered a distinct category of patients.^{5–7} Consequently, patients with a first episode and patients with recurrent pain can be regarded as having similar characteristics, and those with continuous pain symptoms, without periods of very low or no pain, can be classified as the chronic pain group. Differentiating these pain groups is vital for intervention studies, as including NSNP patients showing a recurrent pain pattern may lead to biased outcomes in studies of pain modification, as they might be in a phase of pain relief or exacerbation. Such periods are unlikely in patients with continuous chronic pain. Therefore, it is crucial to handle these groups carefully; either study outcomes should be measured at multiple time points, or a distinction should be made between the subgroups when analyzing the results of effect studies.

In addition, it is important to establish uniformity in research methodology for classifying patients with chronic pain. Establishing a minimal cutoff point for musculoskeletal pain in the ICD-11 would be beneficial rather than merely recommending its incorporation into study descriptions, as currently suggested.^{8,9} A minimal pain cutoff point is expected to ensure that a certain degree of pain

automatically reflects its impact on mental health and/or disability, both of which should be considered when diagnosing chronic primary pain.⁸ However, the optimal cutoff point remains debatable based on the literature and our study.^{10–12} Therefore, it is advisable to investigate the optimal cutoff point to ensure the impact on daily activities and mental health based on a pain cutoff point. This should be included in the definition and subsequently considered in studies on chronic pain.

The prognostic study assessed candidate prognostic factors using questionnaires selected based on their validity, reliability, and practical usability.^{13–25} However, not all questionnaires have been validated for patients with (sub)acute neck pain, such as the Pain Catastrophizing Questionnaire, the Self-Efficacy Scale, and the Tampa Scale of Kinesiophobia, which are more commonly validated for chronic pain conditions.^{14,15,26} Consequently, their psychometric properties cannot be directly extrapolated to the patient category examined in this study.

Furthermore, in selecting an appropriate measure for assessing disability, the Pain Disability Index (PDI) was preferred over the Neck Disability Index (NDI).²⁷ While the NDI assesses a broad spectrum of factors, including limitations in activity, pain, concentration, and sleep quality, it extends beyond our focused definition of disability.²⁸ In contrast, the PDI more accurately matches our definition, emphasizing participation in valued social roles, self-care, and life-support activities.²⁹ However, on questionnaires, individuals with neck pain often do not report significant limitations in daily life.³⁰ It is worth noting that the PDI's generic scope might overlook specific activities that put more strain on the neck, such as lifting or activities that specifically require neck rotation (e.g. cycling or driving a car), potentially underestimating the experienced disability. This highlights the importance of selecting a measurement instrument that accurately reflects the functional limitations of the target population.³¹ A more specific questionnaire for neck pain could potentially reveal higher disability scores. Using a patient-specific approach to measuring activities in which patients feel disabled could offer clearer insights into the impact of sub(acute) neck pain on daily activities.³²

Some candidate prognostic factors were identified, including the ability to change position regularly during work hours and engage in physical activity. However, our measurement method relied heavily on subjective assessments. The ability to change posture at work was evaluated with the question: “Are you able to change positions regularly during your work?”. The limitation of this subjective measurement lies in its inability to clearly distinguish whether individuals perceive

that they can change positions during work, or that they report whether they are actually changing their position. And another problem with this type of questioning is that we cannot confirm e.g. if a patient reports that he/she cannot change position, this is actually true. Similarly, physical activity was measured based on self-reported compliance with the Dutch Healthy Exercise Norm. These subjective evaluations may not accurately reflect the actual activity patterns of participants, underscoring the limitations of self-report measures to accurately capture either sedentary behavior or active behavior.^{33,34} Objective methods, such as accelerometers or physical activity meters, are recommended to measure physical activity and movement patterns at work more accurately.^{33,34} Cross-sectional evidence has linked prolonged computer use and self-reported workplace sitting time to neck pain.^{35,36} Interestingly, the self-perceived ability to modify posture during work was not a significant prognostic factor in the univariable analysis, indicating that this factor has no strong association with the chronification of pain. However, our multivariable prognostic model included the self-perceived ability to modify posture. Although this variable was not significant in the model, this factor added value to the strongest possible model in conjunction with other variables. Given the varying findings in the literature and the results of our prognostic study, it is necessary to reevaluate our measurement approach. A combination of validated objective and subjective measurement approaches would provide broader insights. Establishing the validity and discriminative ability between different concepts being tested is important to investigate before using them in a prognostic study. This is essential to determine how to handle these different measurement outcomes in the analyses.

In the univariable analyses, a variety of psychological factors and illness perceptions demonstrated significantly positive associations with the chronification of pain, including higher scores on catastrophizing, depression, and distress. The multivariable prognostic model further identified both overlapping and unique factors that are prognostic for the chronification of pain. Overlapping factors included higher scores on illness perceptions concerning recovery (specifically regarding concerns and duration) and lower treatment beliefs. Unique to the model were pain self-efficacy and illness beliefs about pain identity. These factors were identified using specific questionnaires designed and validated to measure these constructs.^{20,37} A thorough assessment of these prognostic factors is important as it gives the physiotherapist insights into the clinical presentation of the whole patient. It is essential for facilitating the tailoring of interventions to individuals' needs and guiding referrals to appropriate specialists.

Lastly, the prognostic model developed in our study is not yet generalizable beyond physiotherapy practices, such as general practitioner (GP) practices. This model was constructed using data from initial assessments at primary physiotherapy practices; patients who visit a GP practice represent a subpopulation of patients with neck pain, potentially exhibiting different pain intensities and perceptions about recovery or treatment options. Consequently, applying this prognostic model to GP practices required validation in these settings.

The applicability of our prognostic model within physiotherapy settings seems promising. The identified prognostic factors, outcomes, and reproducible measurements are valuable in clinical practice. Furthermore, models become more generalizable when the range of prognostic values in the new population aligns with those observed in the development population.³⁸ Therefore, given our broad inclusion of various physiotherapy practices and physiotherapists, we are optimistic about external validation and generalizability across different physiotherapy settings. Considering this, it is important to initiate an external validation study. If the model demonstrates good calibration and discriminative ability, it can be implemented in physiotherapy practice. Additionally, validation within GP practices can facilitate clinical decision-making regarding referral to a physiotherapist, psychologist, or specialized rehabilitation clinician to address the patient's prognostic factors before a patient develops chronic pain.

The qualitative study (**Chapter 7**) used semi-structured interviews with a small population. Although saturation was achieved, further exploration would be beneficial. A study that provides deeper insights into the behaviors of physiotherapists while engaging with this patient group through video or audio recordings could be very valuable. The inability of participants to explicitly describe during interviews what actions they take regarding psychosocial prognostic factors – specifically, how to diagnose and modify these factors – highlights a complexity beyond merely possessing and employing skills in this area, whether consciously or unconsciously. Based on this study and existing knowledge on behavior change, interventions for physiotherapists should be targeted towards identifying and addressing facilitators and barriers that affect their ability to incorporate the psychosocial aspect into their clinical practices.³⁹

Further research

In the context of prognostic research on the chronification of pain, it is essential to measure the outcome variable “pain” at multiple time points, given the persistent nature and substantial disease burden of chronic pain. This burden is particularly pronounced in patients who experience constant pain, unlike those who have recurrent pain characterized by periods of relief. I strongly advocate for standardizing the definition of chronicity across all prognostic and effect studies. As described in this dissertation, if pain is present at all measurement moments, i.e. six weeks, three months, and six months, with a Numeric Pain Rating score of three or higher, it should be classified as chronic pain.^{40–42} This standardized definition is important for distinguishing between chronic and recurrent pain conditions, which are associated with different clinical profiles and treatment needs. Implementing this uniform definition would enhance uniformity in research methodologies, thereby increasing the likelihood of developing more accurate prognostic models and achieving consensus among researchers. Moreover, such uniformity facilitates collaboration among research groups, enabling the construction of robust models by integrating more comprehensive data sets.

Additionally, we specifically included potentially modifiable factors in our prognostic analysis. These factors proved individually prognostic in univariable analyses, and some modifiable factors were included within our well-performing, internally validated multivariable model. Despite these promising results, we cannot yet assert that modifying these factors will influence the outcomes, underscoring the need for further research to substantiate these findings. Prognostic research is critical in advancing stratified medicine, which targets treatments based on the risk characteristics shared by patient subgroups. This approach is crucial for identifying priority areas for stratification and discovering candidate factors that may predict treatment response.^{38,43–45} To more effectively advance the potential of prognostic research, our study aligns with recommendations that emphasize the need for rigorous evaluation of factors predicting differential treatment response, ideally through matched care.^{46,47} This can be achieved using Replicated Multiple Single-Case Experimental Design (SCED) studies.⁴⁸ The basic principles of SCED involve repeated measurements, replicating conditions, and analyzing effects concerning each individual, who serves as their own control.^{48,49} This process is useful in identifying the optimal treatment for the individual.^{49,50} This could further substantiate the role of our prognostic model in improving clinical decision-making

and patient outcomes in various healthcare settings, thereby contributing to the broader implementation of matched care approaches in practice.⁴⁶

Prognostic research, including this dissertation, focused primarily on examining factors negatively impacting prognoses. However, further research should also consider more positive factors that serve as protective factors for chronification.⁵¹ These factors could potentially reduce the risk of chronicity, and several of them might also be viewed as modifiable.⁵¹ Consideration can be given to attributes such as resilience, a sense of purpose, adaptability, cognitive and behavioral flexibility, optimism, self-regulation, self-perceived ability to change body position, social connectedness, lifestyle balance, and healthy living habits.^{52,53}

Valorization and clinical implications

Moving to a psychologically informed physiotherapist in primary care

This dissertation emphasizes the need and potential for physiotherapists to incorporate a psychologically informed approach in assessing patients with acute and subacute neck pain. As highlighted in **Chapter 5**, understanding the psychological aspects of neck pain is essential for accurately predicting patient outcomes. The results of this study build upon existing literature to stress the impact of maladaptive cognitions, beliefs, and emotions on the persistence of spinal pain and disability.^{54,55} Occupying a pivotal role as intermediaries between biomedical and psychosocial models, physiotherapists can serve as a bridge between these models, facilitating a comprehensive understanding of how psychological factors interact with a physical condition to influence pain persistence.

Despite these insights, physiotherapists still tend to deal with the more mechanical aspects of neck pain, and they lack confidence and competence in tackling its psychological and social components, as described in **Chapter 7**. This gap underscores the importance of enhancing physiotherapists' training and mentorship to ensure a balanced focus on mechanical and psychological factors in patient care.

This dissertation calls for guideline developers in the neck pain domain to emphasize identifying psychosocial factors.^{40,56} This includes not merely cataloguing these elements as prognostic factors but also delineating specific assessment techniques and the requisite physiotherapist behaviors and interpersonal skills essential to adequately deliver this personalized and matched care approach.

While prevalent in managing musculoskeletal chronic pain, the recognition of psychologically informed practice reveals a notable deficiency in its application to the acute and subacute phases, suggesting a significant area for enhancement in current physiotherapeutic practices. Our study findings reveal that, although patients score on average low on questionnaires assessing psychosocial factors, a small but important number of participants with higher scores demonstrate a significant association with an increased risk of chronicity. Therefore, guidelines must recognize and prioritize the identification and intervention for this specific group to ensure targeted treatment. Further research is necessary to determine whether addressing these factors positively influences the outcome.

Advancing this necessary paradigm shift within our profession, the involvement of professional associations such as the Royal Dutch Society for Physiotherapy (KNGF) and the Quality Register for Physiotherapy (KRF) is vital. The Individual Healthcare Professions (BIG) Act mandates that every physiotherapist must register and continually uphold high professional standards, thereby maintaining the quality of Dutch healthcare and protecting patients from incompetent and negligent practices.⁵⁷ Remarkably, despite the recognized importance of psychosocial factors in physiotherapy, there is no specific guidance on the mandatory educational content for each therapist. This lack of direction may perpetuate a biomedical orientation among therapists, reinforcing continuous confirmation bias. It is recommended that registration bodies mandate a balanced educational approach encompassing biomedical and psychosocial perspectives, thereby fostering a paradigm shift.

Moreover, additional treatment sessions may be necessary to adequately address these complexities when a more psychosocial analysis highlights the existence of these factors. Consequently, insurers in the Netherlands must facilitate the implementation of personalized care within the psychosocial realm of physiotherapy, potentially leading to improved long-term patient outcomes.

Integrating the biopsychosocial model into Bachelor and Master programs in physiotherapy curricula is notable, yet its translation into clinical practice remains suboptimal.^{39,58} This discrepancy underscores the need for ongoing professional development and alignment of educational strategies with actual practice requirements, fostering a more holistic approach in clinical settings.

Finally, the setting of a physiotherapy practice plays a pivotal role in this paradigm shift. The environment significantly influences a physiotherapist's professional

behavior.^{39,59,60} Stimuli from practice owners and observations and experiences with colleagues who embody the role of psychologically informed physiotherapists can profoundly affect the behaviors of other practitioners.³⁹ For professionals to modify their behavior, they require validation, which direct contact with colleagues, peer consultations, or through mandatory internships could provide. Although intervision is currently utilized by professional associations as a tool, it often focuses on discussing case studies and sharing knowledge, which risks fostering a culture of confirmation bias. Awareness surely increases if peer consultation also strives to support physiotherapists to develop towards a psychologically informed practitioner. However, as outlined in the literature³⁹ and discussed in **Chapter 5**, only awareness does not directly impact the actual behavior of physiotherapists.

Integrating prognosis, prognostic factors, and a prognostic model in physiotherapy primary care

The prognostic model developed and validated in **Chapter 5** provides physiotherapists with a robust tool to estimate the likelihood of a patient developing chronic neck pain with a degree of acceptable precision. This model not only allows physiotherapists to discriminate between poor or good prognoses but also highlights that only about 10% of patients may develop chronic pain. This knowledge advocates for a more critical and individualized approach to physiotherapy. It encourages therapists to analyze the necessity and extent of treatments, potentially leading to more efficient use of resources and enhanced patient care. Significantly, this evidence-based knowledge can also help alleviate patients' concerns about the duration of their pain by demonstrating that the probability of developing chronic continuous pain is very low.

Moreover, the results described in **Chapter 5** clarify the prognostic factors that physiotherapists should assess to make informed prognostic judgements. Such insights can refine the initial assessment phase, guiding therapists on which factors are pivotal in forecasting the prognosis. This model is instrumental in enhancing clinical decision-making processes and, in addition, could inform the therapeutic approach, suggesting that modifying certain variables might influence the outcome, i.e., the chronicity of neck pain. However, it is acknowledged that further research is required to conclusively determine the impact of modifying these variables on the outcome of chronic illness.

An external validation study is crucial to bolster the generalizability and reliability of these findings. Continued data collection in diverse physiotherapeutic settings, among general practitioners and in international consortia will be essential to validate the prognostic model across different clinical environments. Additionally, conducting an impact study to assess the practical value and effectiveness of the model in real-world settings will provide critical insights into its utility and potential adjustments needed to enhance predictive accuracy and clinical relevance.

Impact

This study has the potential to significantly influence future prognostic research on neck pain. Notably, our GitHub publication, which includes R scripts and patient data, is freely accessible and facilitates further research. This project has four other significant impacts, which are outlined below.

Knowledge, personal development, and education program

Numerous students participated in this project, with contributions from six students in the qualitative study (**Chapter 7**) from the Master programs in Psychosomatic and the Bachelor program in Physiotherapy. Meanwhile, the cohort study (**Chapter 5**) involved 34 students from the Master programs in Orthopedic Manual Therapy and Psychosomatic Physiotherapy. This engagement resulted in 40 Bachelor and Master thesis projects, providing valuable personal insights for the students and enriching their peers and instructors during the presentation of their theses.

Master students also engaged colleagues from their clinical practices in the data collection process, facilitating the prompt dissemination of initial findings within 30 physiotherapy practices and among 94 physiotherapists. This method of collecting reliable targeted patient data from a specific patient group, combined with the educational benefits for the students, exemplifies a practice that should be more widely adopted in physiotherapy.

Furthermore, this project significantly enhanced the research skills and investigative mindset of the involved physiotherapy students and practitioners. Emphasizing the importance of assembling larger datasets has become increasingly recognized as crucial for improving individual patient care. The approach demonstrated in this study sets a precedent that is likely to inspire future standards in physiotherapy

research and practice, advocating for greater integration of research-oriented methodologies within clinical settings. The new knowledge generated from these studies has been extensively integrated into the curriculum of the master's programs at the University of Applied Sciences Utrecht. It will be further incorporated into the bachelor's program. This integration combines knowledge from these studies with existing literature and translates it into clinical reasoning for patients with musculoskeletal complaints.

Knowledge from these studies has been integrated into a specially designed PAIN course that facilitates the transition from a therapeutic biomedical perspective to a more biopsychosocial perspective and clinical behavior within physiotherapy. **Chapter 7** provides insights into the opportunities for change available to physiotherapists. **Chapters 2** through **Chapter 6** form the substantive background, where not only knowledge is transferred, but special attention is paid to the internalization of practices from a biopsychosocial approach to treating patients with pain complaints. The effectiveness of this course in changing practices is being researched. An elective module will also be offered in the Master's program in Physiotherapy that provides a similar trajectory.

Expansion of prognostic factors in physiotherapy guidelines

Physiotherapy guidelines increasingly emphasize the importance of prognostic factors in managing musculoskeletal complaints. This trend is extensively established and defined within the guidelines for low back pain.⁶¹ Although present, the guidelines concerning neck pain are still in their preliminary stages regarding prognostic elements. This study is poised to offer substantial value when these updated KNGF guidelines provide robust evidence to enhance their comprehensiveness. The findings from these studies will be incorporated into the updated neck pain guidelines and disseminated across the physiotherapy field through webinars and e-learning. Thus, implementation will be concretely executed via the neck pain guideline, directly impacting clinical practice.

Additionally, prognostics and prediction are gaining prominence in clinical reasoning within educational settings. This study contributes to this evolving educational focus, offering deeper insights and practical tools for application. This research enriches the academic curriculum and clinical practice by addressing the practical applicability of prognostic factors, ensuring that future physiotherapists are well-prepared to integrate these elements into patient care.

Neck pain prognostic web application

All patients included in the study are visualized in a web application that integrated our prognostic model and its underlying formulas. This web application allows for deep, patient-level insight from our prognostic model. Moreover, it represents a concrete step towards the future utility of prognostic models in clinical settings, where characteristics of physiotherapy patients can be entered to estimate the probability of chronicity. Such advancements could be integrated into patient tracking systems, enhancing clinical reasoning and (shared-)decision-making in physiotherapy. Importantly, this initiative must be followed up after external validation of the prognostic model, but the initial steps have been successfully implemented within this project. Additionally, the model is designed to allow patients to complete relevant questionnaires before consultations, enabling the physiotherapist to extract a risk percentage for chronicity beforehand. This underscores the practical applicability of the prognostic model for physiotherapists and enhances patient engagement and personalized care.

Initiation of further research projects

This project has yielded valuable data and new insights, which will lead to the initiation of further research projects that will focus on (1) external validation of this prognostic model and its implementation in physiotherapy practice and (2) actual physiotherapeutic treatment within this patient group (PAINCARE). The data we have collected will provide us with a deeper understanding of the phenotypes within this group, which can be distilled from baseline data and the pain outcomes observed in the various follow-up measurements. These phenotypes offer insights for the development of targeted psychosocial therapeutic interventions. From here, we will implement SCED studies within this field to compare standard therapy with the developed treatment strategy for each phenotype. This will operationalize personalized care in physiotherapy for patients with neck pain.

References

1. Treede R-D, Rief W, Barke A, et al. A classification of chronic pain for ICD-11. *Pain*. 2015;156:1003–7. doi: 10.1097/j.pain.000000000000160
2. Hill J, Lewis M, Papageorgiou AC, et al. Predicting Persistent Neck Pain: A 1-year follow-up of a population cohort. *Spine (Phila Pa 1976)*. 2004;29:1648–54. doi: 10.1097/01.BRS.0000132307.06321.3C
3. Pool JJM, Ostelo RWJG, Knol D, et al. Are psychological factors prognostic indicators of outcome in patients with sub-acute neck pain? *Man Ther*. 2010;15:111–6. doi: 10.1016/j.math.2009.08.001
4. Hoving JL, De Vet HCW, Twisk JWR, et al. Prognostic factors for neck pain in general practice. *Pain*. 2004;110:639–45. doi: 10.1016/j.pain.2004.05.002
5. Miró J, de la Vega R, Solé E, et al. Defining mild, moderate, and severe pain in young people with physical disabilities. *Disabil Rehabil*. 2017;39:1131–5. doi: 10.1080/09638288.2016.1185469
6. Gerhart JI, Burns JW, Bruehl S, et al. Variability in negative emotions among individuals with chronic low back pain: relationships with pain and function. *Pain*. 2018;159:342–50. doi: 10.1097/j.pain.0000000000001102
7. Woby SR, Roach NK, Urmston M, et al. The relation between cognitive factors and levels of pain and disability in chronic low back pain patients presenting for physiotherapy. *European Journal of Pain*. 2007;11:869–77. doi: 10.1016/j.ejpain.2007.01.005
8. Nicholas M, Vlaeyen JWS, Rief W, et al. The IASP classification of chronic pain for ICD-11: chronic primary pain. *Pain*. 2019;160:28–37. doi: 10.1097/j.pain.0000000000001390
9. Smith BH, Fors EA, Korwisi B, et al. The IASP classification of chronic pain for ICD-11: applicability in primary care. *Pain*. 2019;160:83–7. doi: 10.1097/j.pain.0000000000001360
10. Woo A, Lechner B, Fu T, et al. Cut points for mild, moderate, and severe pain among cancer and non-cancer patients: a literature review. *Ann Palliat Med*. 2015;4:176–83. doi: 10.3978/j.issn.2224-5820.2015.09.04
11. Boonstra AM, Stewart RE, Albère AJ, et al. Cut-offpoints for mild, moderate, and severe pain on the numeric rating scale for pain in patients with chronic musculoskeletal pain: Variability and influence of sex and catastrophizing. *Front Psychol*. 2016;7. doi: 10.3389/fpsyg.2016.01466
12. Hirschfeld G, Zernikow B. Variability of ‘optimal’ cut points for mild, moderate, and severe pain: neglected problems when comparing groups. *Pain*. 2013;154:154–9. doi: 10.1016/j.pain.2012.10.008
13. Pollard CA. Preliminary validity study of the pain disability index. *Percept Mot Skills*. 1984;59:974. doi: 10.2466/pms.1984.59.3.974
14. McWilliams LA, Kowal J, Wilson KG. Development and evaluation of short forms of the Pain Catastrophizing Scale and the Pain Self-efficacy Questionnaire. *European Journal of Pain (United Kingdom)*. 2015;19:1342–9. doi: 10.1002/ejp.665
15. Woby SR, Roach NK, Urmston M, et al. Psychometric properties of the TSK-11: A shortened version of the Tampa Scale for Kinesiophobia. *Pain*. 2005;117:137–44. doi: 10.1016/j.pain.2005.05.029

- 16 Bijker L, Sleijser-Koehorst MLS, Coppieters MW, et al. Preferred Self-Administered Questionnaires to Assess Depression, Anxiety and Somatization in People With Musculoskeletal Pain – A Modified Delphi Study. *Journal of Pain*. 2020;21:409–17. doi: 10.1016/j.jpain.2019.08.006
- 17 de Beurs E, Van Dyck R, Marquenie LA, et al. De DASS: een vragenlijst voor het meten van depressie, angst en stress. *Gedragstherapie*. 2001;34:35–54.
- 18 Kraaiaat FW, Evers AWM. Pain-Coping Strategies in Chronic Pain Patients: Psychometric Characteristics of the Pain-Coping Inventory (PCI). *Int J Behav Med*. 2003;10:343–63. doi: 10.1207/S15327558IJBM1004_5
- 19 Brown GK, Nicassio PM. Development of a questionnaire for the assessment of active and passive coping strategies in chronic pain patients. *Pain*. 1987;31:53–64. doi: 10.1016/0304-3959(87)90006-6
- 20 de Raaij EJ, Schröder C, Maissan FJ, et al. Cross-cultural adaptation and measurement properties of the Brief Illness Perception Questionnaire-Dutch Language Version. *Man Ther*. 2012;17:330–5. doi: 10.1016/j.math.2012.03.001
- 21 Moss-Morris R, Weinman J, Petrie K, et al. The revised Illness Perception Questionnaire (IPQ-R). *Psychol Health*. 2002;17:1–16. doi: 10.1080/08870440290001494
- 22 Kunz M, Capito ES, Horn-Hofmann C, et al. Psychometric Properties of the German Version of the Pain Vigilance and Awareness Questionnaire (PVAQ) in Pain-Free Samples and Samples with Acute and Chronic Pain. *Int J Behav Med*. 2017;24:260–71. doi: 10.1007/s12529-016-9585-4
- 23 Roelofs J, Peters ML, Muris P, et al. Dutch version of the Pain Vigilance and Awareness Questionnaire: Validity and reliability in a pain-free population. *Behaviour Research and Therapy*. 2002;40:1081–90. doi: 10.1016/S0005-7967(02)00008-6
- 24 Sleijser-Koehorst MLS, Bijker L, Cuijpers P, et al. Preferred self-administered questionnaires to assess fear of movement, coping, self-efficacy, and catastrophizing in patients with musculoskeletal pain - A modified Delphi study. *Pain*. 2019;160:600–6. doi: 10.1097/j.pain.0000000000001441
- 25 Nicholas MK, McGuire BE, Asghari A. A 2-item short form of the pain self-efficacy questionnaire: Development and psychometric evaluation of PSEQ-2. *Journal of Pain*. 2015;16:153–63. doi: 10.1016/j.jpain.2014.11.002
- 26 Dubé M-O, Langevin P, Roy J-S. Measurement properties of the Pain Self-Efficacy Questionnaire in populations with musculoskeletal disorders: a systematic review. *Pain Rep*. 2021;6:e972. doi: 10.1097/PR9.0000000000000972
- 27 Ailliet L, Knol DL, Rubinstein SM, et al. Definition of the construct to be measured is a prerequisite for the assessment of validity. The Neck Disability Index as an example. *J Clin Epidemiol*. 2013;66:775–82.e2. doi: 10.1016/j.jclinepi.2013.02.005
- 28 Vernon H, Mior S. The Neck Disability Index: a study of reliability and validity. *J Manipulative Physiol Ther*. 1991;14:409–15.
- 29 Tait RC, Chibnall JT, Krause S. The Pain Disability Index: psychometric properties. *Pain*. 1990;40:171–82. doi: 10.1016/0304-3959(90)90068-O
- 30 Fejer R, Hartvigsen J. Neck pain and disability due to neck pain: what is the relation? *European Spine Journal*. 2008;17:80–8. doi: 10.1007/s00586-007-0521-9
- 31 Howell ER. The association between neck pain, the Neck Disability Index and cervical ranges of motion: a narrative review. *J Can Chiropr Assoc*. 2011;55:211–21.

- 32 Beurskens AJ, de Vet HC, Kökeb AJ, et al. A patient-specific approach for measuring functional status in low back pain. *J Manipulative Physiol Ther.* 1999;22:144–8. doi: 10.1016/S0161-4754(99)70127-2
- 33 van Weering M, Vollenbroek-Hutten M, Hermens H. The relationship between objectively and subjectively measured activity levels in people with chronic low back pain. *Clin Rehabil.* 2011;25:256–63. doi: 10.1177/0269215510380828
- 34 Vergauwen K, Huijnen IPJ, Smeets RJEM, et al. An exploratory study of discrepancies between objective and subjective measurement of the physical activity level in female patients with chronic fatigue syndrome. *J Psychosom Res.* 2021;144:110417. doi: 10.1016/j.jpsychores.2021.110417
- 35 Demissie B, Bayih ET, Demmelash AA. A systematic review of work-related musculoskeletal disorders and risk factors among computer users. *Heliyon.* 2024;10:e25075. doi: 10.1016/j.heliyon.2024.e25075
- 36 Kallings LV, Blom V, Ekblom B, et al. Workplace sitting is associated with self-reported general health and back/neck pain: a cross-sectional analysis in 44,978 employees. *BMC Public Health.* 2021;21:875. doi: 10.1186/s12889-021-10893-8
- 37 de Raaij EJ, Schröder C, Maissan FJ, et al. Cross-cultural adaptation and measurement properties of the Brief Illness Perception Questionnaire-Dutch Language Version. *Man Ther.* 2012;17:330–5. doi: 10.1016/j.math.2012.03.001
- 38 Moons KGM, Altman DG, Vergouwe Y, et al. Prognosis and prognostic research: application and impact of prognostic models in clinical practice. *BMJ.* 2009;338:b606–b606. doi: 10.1136/bmj.b606
- 39 van Dijk H, Köke AJA, Elbers S, et al. Physiotherapists Using the Biopsychosocial Model for Chronic Pain: Barriers and Facilitators—A Scoping Review. *Int J Environ Res Public Health.* 2023;20:1634. doi: 10.3390/ijerph20021634
- 40 Traeger A, Henschke N, Hübscher M, et al. Development and validation of a screening tool to predict the risk of chronic low back pain in patients presenting with acute low back pain: a study protocol. *BMJ Open.* 2015;5:e007916. doi: 10.1136/bmjopen-2015-007916
- 41 Kamper SJ, Maher CG, Herbert RD, et al. How little pain and disability do patients with low back pain have to experience to feel that they have recovered? *Eur Spine J.* 2010;19:1495–501. doi: 10.1007/s00586-010-1366-1
- 42 Verwoerd MJ, Wittink H, Maissan F, et al. A study protocol for the validation of a prognostic model with an emphasis on modifiable factors to predict chronic pain after a new episode of acute- or subacute nonspecific idiopathic, non-traumatic neck pain presenting in primary care. *PLoS One.* 2023;18:e0280278. doi: 10.1371/journal.pone.0280278
- 43 Hingorani AD, Van Der Windt DA, Riley RD, et al. Prognosis research strategy (PROGRESS) 4: Stratified medicine research. *BMJ (Online).* 2013;346:1–9. doi: 10.1136/bmj.e5793
- 44 Riley RD, Hayden JA, Steyerberg EW, et al. Guidelines and Guidance Prognosis Research Strategy (PROGRESS) 2: Prognostic Factor Research. *PLoS Med.* 2013;10:e1001380. doi: 10.1371/journal.pmed.1001380
- 45 Steyerberg, EW, Moons, KGM, van der Windt, DA, Hayden, JA, Perel, P et al. Prognosis Research Strategy (PROGRESS) 3: Prognostic Model Research. *PLoS Med.* 2013;10(2). doi: <https://doi.org/10.1371/journal.pmed.1001381>
- 46 Linton SJ, Nicholas M, Shaw W. Why wait to address high-risk cases of acute low back pain? A comparison of stepped, stratified, and matched care. *Pain.* 2018;159:2437–41. doi: 10.1097/j.pain.0000000000001308

- 47 McCracken LM. Personalized pain management: Is it time for process-based therapy for particular people with chronic pain? *European Journal of Pain*. 2023;27:1044–55. doi: 10.1002/ejp.2091
- 48 Onghena P, Edgington ES. Customization of Pain Treatments. *Clin J Pain*. 2005;21:56–68. doi: 10.1097/00002508-200501000-00007
- 49 Davidson KW, Silverstein M, Cheung K, et al. Experimental Designs to Optimize Treatments for Individuals. *JAMA Pediatr*. 2021;175:404. doi: 10.1001/jamapediatrics.2020.5801
- 50 Dallery J, Raiff BR. Optimizing behavioral health interventions with single-case designs: from development to dissemination. *Transl Behav Med*. 2014;4:290–303. doi: 10.1007/s13142-014-0258-z
- 51 Braunwalder C, Müller R, Glisic M, et al. Are Positive Psychology Interventions Efficacious in Chronic Pain Treatment? A Systematic Review and Meta-Analysis of Randomized Controlled Trials. *Pain Medicine*. 2022;23:122–36. doi: 10.1093/pm/pnab247
- 52 O’Sullivan PB, Caneiro JP, O’Keeffe M, et al. Cognitive Functional Therapy: An Integrated Behavioral Approach for the Targeted Management of Disabling Low Back Pain. *Phys Ther*. 2018;98:408–23. doi: 10.1093/ptj/pzy022
- 53 Sturgeon JA, Zautra AJ. Resilience: a new paradigm for adaptation to chronic pain. *Curr Pain Headache Rep*. 2010;14:105–12. doi: 10.1007/s11916-010-0095-9
- 54 Martinez-Calderon J, Flores-Cortes M, Morales-Asencio JM, et al. Which Psychological Factors Are Involved in the Onset and/or Persistence of Musculoskeletal Pain? An Umbrella Review of Systematic Reviews and Meta-Analyses of Prospective Cohort Studies. *Clin J Pain*. 2020;36:626–37. doi: 10.1097/AJP.0000000000000838
- 55 Nieminen LK, Pyysalo LM, Kankaanpää MJ. Prognostic factors for pain chronicity in low back pain: a systematic review. *Pain Rep*. 2021;6:e919. doi: 10.1097/PR9.0000000000000919
- 56 National Institute for Health and Care Excellence (NICE). *Low Back Pain and Sciatica in Over 16s: Assessment and Management*. London 2016.
- 57 Laws and regulations | Registration | BIG-register (bigregistr.nl). <https://english.bigregister.nl/>.
- 58 Smart KM. The biopsychosocial model of pain in physiotherapy: past, present and future. *Physical Therapy Reviews*. 2023;28:61–70. doi: 10.1080/10833196.2023.2177792
- 59 Gleadhil C, Bolsewicz K, Davidson SRE, et al. Physiotherapists’ opinions, barriers, and enablers to providing evidence-based care: a mixed-methods study. *BMC Health Serv Res*. 2022;22:1382. doi: 10.1186/s12913-022-08741-5
- 60 Delany C, Edwards I, Fryer C. How physiotherapists perceive, interpret, and respond to the ethical dimensions of practice: A qualitative study. *Physiother Theory Pract*. 2018;1–14. doi: 10.1080/09593985.2018.1456583
- 61 KNGF/VvOCM. *The KNGF Guideline on Low Back Pain and Lumbosacral Radicular Syndrome*. Amersfoort/Utrecht 2021.





Summary

The main aim of this thesis was to research the prognostic factors involved in the development of chronic non-specific neck pain (NSNP) and to develop a prognostic model that will enable better prediction of which patients are at risk of developing chronic pain. Additionally, this research explores physiotherapists' knowledge, attitude, and practice behaviors in managing (sub)acute NSNP.

PART 1 of this thesis starts with a systematic review in **CHAPTER 2**, identifying prognostic factors for the persistence of pain and perceived non-recovery following an episode of NSNP. A comprehensive literature search, encompassing studies up to October 21, 2017, focused on prospective prognostic studies evaluating pain intensity and perceived non-recovery. Quality assessment was conducted using the Quality in Prognostic Studies (QUIPS) tool. Six prospective studies were included out of 2,737 articles screened, analyzing 47 and 43 factors for pain intensity and perceived non-recovery, respectively. Moderate evidence suggested that age over 40 years and accompanying back pain are prognostic for persistent pain intensity. For perceived non-recovery at 12 months, previous neck pain episodes and accompanying headaches showed moderate evidence as prognostic factors. However, the quality of evidence was rated as low to very low.

Following the systematic review revealing low-quality evidence for prognostic factors in non-specific, non-traumatic neck pain, **CHAPTER 3** aimed to identify and establish a consensus on potential prognostic factors, particularly those modifiable by physiotherapy. Employing a modified Nominal Group Technique (m-NGT) and a Delphi survey, this study gathered expert input to identify and categorize potential prognostic factors. Conducted from November 2018 to January 2020, the Delphi survey sought expert consensus on the prognostic value of these factors, their modifiability, and measurement methods in clinical practice. The m-NGT meeting initially identified 84 factors, refined to 47 and categorized into 12 groups. The subsequent Delphi survey led to consensus on 25 prognostic factors of chronic idiopathic, non-traumatic neck pain, 19 of which are potentially modifiable through physiotherapy, with a significant number being psychological. This emphasizes the importance of a biopsychosocial approach to further prognostic research.

Transitioning to **PART 2**, the focus shifts from identifying and finding experts' consensus on prognostic factors to empirical research. **CHAPTER 4** outlined a study protocol for the development and internal validation of a prognostic model. This study aimed to identify independent prognostic factors, both modifiable and non-modifiable, for the development of chronic pain in patients with acute or

subacute nonspecific idiopathic, non-traumatic neck pain. This prospective cohort study, conducted between January 2020 and March 2023, involved 30 primary physiotherapy practices and followed patients with a six-month follow-up period, with measurement points at six weeks, three months, and six months. The study uses comprehensive data collection methods, including baseline questionnaires measuring candidate prognostic variables related to symptoms, work, general health, and psychological and behavioral factors. Chronic neck pain was defined as a Numeric Pain Rating Scale (NPRS) score of ≥ 3 at six weeks, three months and six months. The statistical analysis in this study was conducted according to the Prognosis Research Strategy (PROGRESS) framework, specifically type 3 research. Advanced statistical analyses were employed to develop and validate the prognostic model, including univariable and multivariable logistic regression and internal validation techniques like bootstrapping. **CHAPTER 5** describes the results of this prognostic study. A total of 603 participants were included after screening 2,567 patients. Out of the participants, 62 (10%) developed chronic pain. The univariable analyses identified significant prognostic factors of pain chronification, including gender (female), baseline pain intensity, pain duration, pain in different body regions, the onset of headache since the neck pain, higher disability scores, unemployment, higher scores on catastrophizing, illness beliefs about recovery (concerned and duration), depression, distress, and lower treatment beliefs. Vital prognostic factors in the final model included sex, pain intensity, pain in different body regions, headaches, ability to modify posture during work, employment status, and several illness beliefs and psychological measures. Knowing illness beliefs about pain identity and recovery, treatment beliefs, distress, and self-efficacy. The model demonstrated good fit and predictive accuracy with an optimism-corrected AUC of 0.83 and a corrected R^2 of 0.24. This study aimed to enhance the understanding of prognostic factors, aiding clinicians in making informed decisions, tailoring individual treatment approaches, and accurately predicting the likelihood of chronic pain development.

CHAPTER 6 aimed to compare the clinical characteristics and recovery rates between patients experiencing their first episode of nonspecific neck pain and those with recurrent episodes. Additionally, the study investigated the differences in daily activities, illness perceptions, and psychological factors between patients with mild pain (1–2 on the Numeric Pain Rating Scale (NPRS)) and those with moderate to severe pain (≥ 3 NPRS) six weeks after their initial presentation in clinical practice. Data from the prognostic study was used. The study cohort

included 198 (33%) individuals experiencing their first episode of (sub)acute neck pain and 405 (67%) with recurrent neck pain. Among the 449 responders at six weeks, 278 participants still reported experiencing neck pain, with a mean intensity of 4.2 (SD = 2.0). The findings indicated no clinically meaningful differences in the clinical characteristics or recovery rates at six weeks, three months, and six months between patients experiencing their first episode of NSNP and those with recurrent episodes. However, significant differences emerged in how mild pain (1–2 NPRS) versus moderate to severe pain (≥ 3 NPRS) impacted disability, patient concerns, and self-efficacy at the six-week mark. Patients with higher pain intensity reported greater disability, higher levels of concern, and lower self-efficacy. Specifically, the differences were clinically meaningful with a 1.33-point difference (SD 0.84–1.81) in disability on a 0–7 scale, a -1.25-point difference (SD -1.84 to -0.65) in self-efficacy on a 0–12 scale, and a 1.87-point difference (SD 1.21–2.52) in patient concerns on a 0–10 scale.

PART 3 shifts the focus to physiotherapists working in primary care. **CHAPTER 7** aimed to explore physiotherapists' knowledge, attitudes, and practice behaviors in managing non-specific, non-traumatic, (sub)acute neck pain, focusing on identifying and modifying prognostic factors for chronic pain. This study utilized semi-structured interviews with 13 primary care physiotherapists, employing qualitative content analysis for data interpretation. In-depth interviews were conducted following the Knowledge-Attitude-Practice (KAP) framework. A purposive sample method was used to capture diverse perspectives. Seven main themes emerged from the analysis: (1) Self-estimated Knowledge and Attitude; physiotherapists recognized the impact of psychosocial factors on neck pain and generally shifted from a biomedical to a biopsychosocial approach over time. (2) Role clarity: there were varied perceptions of role boundaries, with some expanding their roles to include psychosocial aspects. (3) Therapeutic relationships, trust, and cooperation were deemed essential. Physiotherapists often adapted their approach to align with patient expectations. (4) Internal barriers to practice, limited knowledge, and skills in dealing with complex psychosocial factors were noted. (5) External barriers to practice: patients' reluctance to engage in a biopsychosocial approach was a common barrier. (6) Practice behaviors: physiotherapists relied more on experience than structured assessments for psychosocial factors, with a tendency to prioritize physical treatment approaches. (7) Self-reflection: this was considered crucial for professional development and adopting a broader therapeutic perspective. This chapter revealed a complex relationship between physiotherapists' knowledge,

attitudes, and practice behaviors in managing neck pain. Despite a general shift towards a biopsychosocial approach, physiotherapists faced challenges integrating it into their practice, influenced by personal attitudes, patient expectations, and individual competencies. This chapter highlights the need for enhanced training and support in biopsychosocial approaches, emphasizing the role of self-reflection in professional growth and practice improvement.





Nederlandse samenvatting
(Summary in Dutch)

Het primaire doel van dit proefschrift was het onderzoeken van prognostische factoren die een rol spelen bij de ontwikkeling van chronische niet-specifieke nekpijn (NSNP) en het ontwikkelen van een prognostisch model dat accuraat voorspelt welke patiënten risico lopen op het ontwikkelen van chronische pijn. Daarnaast werd de kennis, attitude en het gedrag van fysiotherapeuten in de eerstelijnszorg onderzocht met betrekking tot het klinische handelen bij patiënten met (sub)acute NSNP.

DEEL 1 van dit proefschrift begint met een systematische review in **HOOFDSTUK 2**, gericht op het identificeren van prognostische factoren voor het aanhouden van pijn en het ervaren van onvoldoende herstel na een episode van idiopathische, niet-traumatische nekpijn. Een literatuuronderzoek, dat studies tot 21 oktober 2017 omvatte, was gericht op prospectieve prognostische studies die pijnintensiteit en het ervaren van onvoldoende herstel beoordeelden. De kwaliteit van deze studies werd beoordeeld met het Quality in Prognostic Studies (QUIPS) instrument. Van de 2.737 gescreende artikelen werden zes prospectieve studies geïncludeerd, waarin respectievelijk 47 en 43 factoren voor pijnintensiteit en ervaren onvoldoende herstel werden geanalyseerd. Er werd matig bewijs gevonden voor de factoren leeftijd boven de 40 jaar en gelijktijdige rugpijn voor aanhoudende pijn. Voor het ervaren van onvoldoende herstel na 12 maanden werd matig bewijs gevonden voor eerdere episodes van nekpijn en bijkomende hoofdpijn. De kwaliteit van dit bewijs werd echter beoordeeld als laag tot zeer laag.

Na deze systematische review, waarbij beperkt bewijs voor prognostische factoren in specifieke, niet-traumatische nekpijn werd gevonden, richtte **HOOFDSTUK 3** zich op het identificeren en bereiken van consensus over potentiële prognostische factoren, met specifieke aandacht voor factoren die door fysiotherapeutische interventie beïnvloedbaar zijn. Middels een gemodificeerde Nominal Group Technique (m-NGT) en een Delphi-studie werd input van experts verzameld om potentiële prognostische factoren te identificeren en te categoriseren. De Delphi-studie, uitgevoerd van november 2018 tot januari 2020, streefde naar consensus onder experts over de prognostische waarde van deze factoren, hun potentieel beïnvloedbare karakter en meetinstrumenten voor de klinische praktijk. De m-NGT-bijeenkomst identificeerde aanvankelijk 84 factoren, die werden teruggebracht tot 47 en ingedeeld in 12 categorieën. De daaropvolgende Delphi-studie resulteerde in consensus over 25 prognostische factoren voor chronische idiopathische, niet-traumatische nekpijn, waarvan 19 potentieel beïnvloedbaar zijn door fysiotherapie,

met een aanzienlijk aantal van psychologische aard. Dit benadrukt het belang van een biopsychosociale benadering in verder prognostisch onderzoek.

DEEL 2 verschuift de focus van het identificeren en consensus bereiken over prognostische factoren naar empirisch onderzoek. **HOOFDSTUK 4** beschrijft een onderzoeksprotocol voor het ontwikkelen en interne valideren van een prognostisch model. Het doel van deze studie was het identificeren van prognostische factoren, zowel modificeerbaar als niet-modificeerbaar, voor de ontwikkeling van chronische pijn bij patiënten met acute of subacute aspecifieke idiopathische, niet-traumatische nekpijn. Deze prospectieve cohortstudie, uitgevoerd tussen januari 2020 en maart 2023, betrok 30 eerstelijnsfysiotherapiepraktijken en volgde patiënten gedurende een periode van zes maanden, met meetmomenten na zes weken, drie maanden en zes maanden. De studie gebruikte uitgebreide methoden voor gegevensverzameling, waaronder vragenlijsten die potentiële prognostische variabelen konden objectiveren, gerelateerd aan symptomen, werk, algemene gezondheid, en psychologische en gedragsfactoren. Chronische nekpijn werd gedefinieerd als een score van ≥ 3 op de Numeric Pain Rating Scale (NPRS) na zes weken, drie maanden en zes maanden. De statistische analyse was gebaseerd op het Prognosis Research Strategy (PROGRESS) framework, specifiek gericht op type 3-onderzoek. Geavanceerde statistische analyses, waaronder univariabele en multivariabele logistische regressie en interne validatietechnieken zoals bootstrapping, werden ingezet om het prognostisch model te ontwikkelen en te valideren.

HOOFDSTUK 5 beschrijft de resultaten van deze prognostische studie. Van de 2.567 gescreende patiënten werden 603 deelnemers geïncludeerd, waarvan 62 (10%) chronische pijn ontwikkelden. De univariabele analyses identificeerden significante prognostische factoren voor de chronificatie van pijn, waaronder geslacht (vrouw), initiële pijnintensiteit, pijn duur, pijn in verschillende lichaamsregio's, het optreden van hoofdpijn sinds het begin van de nekpijn, meer ervaren beperkingen in activiteiten, arbeidsstatus (niet werken), hogere scores op catastroferen, ziektepercepties over herstel (zorgen en duur), depressie, distress en lagere verwachtingen van de behandeling. Belangrijke prognostische factoren in het uiteindelijke model omvatten geslacht, pijnintensiteit, pijn in verschillende lichaamsregio's, hoofdpijn, het vermogen om de houding tijdens het werk aan te passen, arbeidsstatus, en diverse ziektepercepties en psychologische factoren, te weten, ziektepercepties over de identiteit van de nekpijn en herstel, verwachtingen over de behandeling, distress en zelfeffectiviteit. Het model toonde een goede calibratie en voorspellende

nauwkeurigheid met een optimisme-gecorrigeerde AUC van 0,83 en een gecorrigeerde R^2 van 0,24. Het doel van deze studie was het verbeteren van het inzicht in prognostische factoren, waardoor clinici worden ondersteund bij het nemen van evidente beslissingen, het aanpassen van individuele behandelingsbenaderingen en met name het nauwkeurig voorspellen van de waarschijnlijkheid van het ontwikkelen van chronische pijn.

HOOFDSTUK 6 had als doel de klinische kenmerken en herstelpercentages te vergelijken tussen patiënten die hun eerste episode van niet-specifieke nekpijn ervaren en patiënten met terugkerende episodes. Daarnaast onderzocht de studie de verschillen in dagelijkse activiteiten, ziektepercepties en psychologische factoren tussen patiënten met milde pijn (1–2 op de Numeric Pain Rating Scale (NPRS)) en degenen met matige tot ernstige pijn (≥ 3 NPRS) zes weken na hun eerste presentatie in de klinische praktijk. Gegevens uit de prognostische studie werden gebruikt. De onderzoeksgroep bestond uit 198 (33%) individuen die hun eerste episode van (sub)acute nekpijn ervoeren en 405 (67%) met terugkerende nekpijn. Van de 449 respondenten na zes weken, rapporteerden 278 deelnemers nog steeds nekpijn, met een gemiddelde intensiteit van 4,2 (SD = 2,0). De bevindingen toonden aan dat er geen betekenisvolle verschillen waren in de klinische kenmerken of herstelpercentages na zes weken, drie maanden en zes maanden tussen patiënten die hun eerste episode van niet-specifieke nekpijn ervoeren en degenen met terugkerende episodes. Echter, er kwamen significante betekenisvolle verschillen naar voren in hoe milde pijn (1–2 NPRS) versus matige tot ernstige pijn (≥ 3 NPRS) invloed had op beperkingen in dagelijkse activiteiten, zorgen die patiënten hadden en zelfeffectiviteit na zes weken. Patiënten met een hogere pijnintensiteit rapporteerden meer beperkingen, meer zorgen en een lagere zelfeffectiviteit. Specifiek waren de verschillen klinisch betekenisvol met een verschil van 1,33 punten (SD 0,84–1,81) in beperkingen op een 0–7 schaal, een verschil van -1,25 punten (SD -1,84 tot -0,65) in zelfeffectiviteit op een 0–12 schaal, en een verschil van 1,87 punten (SD 1,21–2,52) in de mate van zorgen op een 0–10 schaal.

DEEL 3 richt de aandacht op fysiotherapeuten werkzaam in de eerstelijnszorg. **HOOFDSTUK 7** exploreerde de kennis, attitude en gedrag van fysiotherapeuten in het klinisch handelen van aspecifieke, niet-traumatische, (sub)acute nekpijn, met specifieke aandacht voor het identificeren en beïnvloeden van prognostische factoren voor chronische pijn. Er werden semi-gestructureerde interviews afgenomen bij 13 eerstelijnsfysiotherapeuten, waarbij kwalitatieve content analyse

werd toegepast voor data-interpretatie. De interviews werden uitgevoerd volgens het Knowledge-Attitude-Practice (KAP) kader, en een doelgerichte steekproefmethode werd gebruikt om een diversiteit aan perspectieven te waarborgen. Uit de analyse kwamen zeven hoofdthema's naar voren: (1) Zelfingeschatte Kennis en Attitude; fysiotherapeuten erkenden de invloed van psychosociale factoren op nekpijn en gingen geleidelijk over van een biomedische naar een biopsychosociale benadering. (2) Rolhelderheid; de percepties over de afbakening van rollen varieerden, waarbij sommigen hun rol uitbreidden om psychosociale aspecten te omvatten. (3) Therapeutische Relatie; vertrouwen en samenwerking werden als essentieel beschouwd, waarbij fysiotherapeuten hun benadering vaak afstemden op de verwachtingen van patiënten. (4) Interne Barrières voor de Praktijk; er was een beperkte kennis en vaardigheid in het omgaan met complexe psychosociale factoren. (5) Externe Barrières voor de Praktijk; de terughoudendheid van patiënten om een biopsychosociale benadering te accepteren was een veelvoorkomende barrière. (6) Praktijkgedrag; fysiotherapeuten vertrouwden meer op ervaring dan op gestructureerde beoordelingen voor psychosociale factoren en neigden naar het prioriteren van fysieke behandelmethoden. (7) Zelfreflectie; dit werd beschouwd als essentieel voor professionele ontwikkeling en het aannemen van een breder therapeutisch perspectief. Dit hoofdstuk onthulde een complexe dynamiek tussen de kennis, houdingen en praktijkgedrag van fysiotherapeuten in het klinische handelen bij nekpijn. Ondanks een algemene verschuiving naar een biopsychosociale benadering, ondervonden fysiotherapeuten uitdagingen bij het integreren van deze benadering in hun praktijk, beïnvloed door persoonlijke attitudes, verwachtingen van patiënten en individuele competenties. Dit hoofdstuk benadrukt de noodzaak van uitgebreidere training en ondersteuning in biopsychosociale benaderingen, met nadruk op de rol van zelfreflectie in de professionele groei en het verbeteren van de praktijkvoering.





Author affiliations

Prof. Dr. Rob J.E.M. Smeets, Department of Rehabilitation Medicine, Research School CAPHRI, Maastricht University, Maastricht, The Netherlands. CIR Clinics in Rehabilitation, CIR, Eindhoven, The Netherlands.

Dr. Harriët Wittink, Research Group Lifestyle and Health, Research Centre Healthy and Sustainable Living, HU University of Applied Sciences Utrecht, Utrecht, The Netherlands.

Dr. Francois Maissan, Research Group Lifestyle and Health, Research Centre Healthy and Sustainable Living, HU University of Applied Sciences Utrecht, Utrecht, The Netherlands.

Dr. Edwin de Raaij, Research Group Lifestyle and Health, Research Centre Healthy and Sustainable Living, HU University of Applied Sciences Utrecht, Utrecht, The Netherlands.

Dr. Sander M.J. van Kuijk, Department of Clinical Epidemiology and Medical Technology Assessments, Maastricht University Medical Centre, Maastricht, The Netherlands.

Marc A.T. Teunis, PhD Research Group Innovative Testing in Life Sciences and Chemistry, Research Centre Healthy and Sustainable Living, University of Applied Sciences Utrecht, Utrecht, The Netherlands.

Dr. Mariëlle E.J.B. Goossens, Department of Rehabilitation Research, Maastricht University, Maastricht, The Netherlands.

Martine Verwoerd, Research Group Lifestyle and Health, Research Centre Healthy and Sustainable Living, HU University of Applied Sciences Utrecht, Utrecht, The Netherlands.





Dankwoord (Acknowledgements)

Als ik van tevoren een prognostisch model had moeten opstellen voor het succesvol afronden van mijn proefschrift, dan zou ik nu precies weten welke variabelen essentieel zouden zijn voor een positieve uitkomst. Deze omvatten onder andere een promotieteam waarop je kunt rekenen, deskundige en inspirerende co-auteurs, een lectoraat waarbinnen je je veilig voelt, collega's die betrokkenheid tonen, lieve vriendinnen die je gelukkig maken, een warme familie, een partner die je steunt en kinderen die zoveel vreugde brengen en voor de nodige afleiding zorgen. Al deze variabelen hebben in belangrijke mate bijgedragen aan mijn ontzettend leuke traject en de uiteindelijke vorming van dit proefschrift.

Als eerste wil ik mijn promotieteam bedanken voor de onmisbare ondersteuning en deskundige begeleiding gedurende de afgelopen jaren. Ik heb mijn team ervaren als stimulerend en kritisch, maar ook als ondersteunend én aangenaam: een ideale combinatie voor mij. In ons team kon ik mezelf zijn en kreeg ik de gelegenheid om mij persoonlijk en professioneel te ontwikkelen.

Rob, ik ben ontzettend blij dat jij mijn promotor bent. De samenwerking met jou was verrijkend, mede doordat je naast een kritische onderzoeker ook over een schat aan praktijkervaring beschikt. Dit heeft de relevantie van ons onderzoek steeds naar een hoger niveau getild. Ik werk graag in de toekomst nog met je verder!

Harriët, je hebt mij veel kansen geboden en onze samenwerking was buitengewoon plezierig. In het proces ben je altijd duidelijk, heel eerlijk en transparant geweest. Ik heb dit enorm gewaardeerd. Als iets goed was, was dat duidelijk. Als iets (nog) niet goed was, hoorde ik dat ook. Ik wist altijd waar ik aan toe was. Deze manier van werken heeft mij geholpen in de onderzoekswereld. Jij hebt mij laten zien hoe uitdagend en leuk een wereld kan zijn waarvan ik vroeger nooit dacht dat ik er enthousiast over zou kunnen worden. Je hebt mij het vertrouwen gegeven dat ik nodig had om mij hierin te ontwikkelen.

Francois, inhoudelijk was je een waardevolle ondersteuning in dit traject. Jouw kennis van de literatuur en het vakgebied was steeds een bron van inspiratie tijdens onze overleggen en discussies. Je stimulerende aanwezigheid en het vermogen om humor in onze bijeenkomsten te brengen, waren voor mij van grote waarde.

Ik wil ook de leden van de beoordelingscommissie bedanken voor hun aandacht en zorgvuldigheid bij het lezen en beoordelen van mijn proefschrift. Ik vind het heel bijzonder dat mijn opponenten vanuit verschillende vakgebieden zoveel tijd en aandacht besteden aan mijn proefschrift.

Daarnaast wil ik al mijn co-auteurs hartelijk danken. Marc Teunis, er is eigenlijk maar één moment in mijn promotietraject geweest waarop ik het écht even niet zag zitten; bij de overstap van SPSS naar R. Jouw enthousiasme, expertise en geduld zijn voor mij cruciaal geweest voor mijn voortgang. Ik had nooit gedacht dat ik kon gaan lachen om R-codes, bijzondere outputs en dat ik het echt zo leuk zou gaan vinden om samen op een zaterdagavond formules en codes uit te vogelen. Sander van Kuijk, jouw komst als expert op het gebied van prognostische modellen was van onmiskenbare hulp. Ik heb echt veel van je geleerd en ik vond de ‘Sander-vragen-uurtjes’ enorm waardevol en plezierig. Na onze overleggen kon ik altijd direct weer een stap verder. Mariëlle Goossens, bedankt dat je deel wilde uitmaken van mijn team voor de kwalitatieve studie. Jouw expertise op het gebied van kwalitatief onderzoek en psychologie hebben bijgedragen aan de kwaliteit van die studie. De kritische vragen hebben mij tijdens die studie scherp gehouden. Edwin de Raaij, bedankt voor het meedenken bij de systematische review. Je was eerst mijn docent bij de Master Manuele Therapie en toen had ik nooit gedacht dat we een aantal jaar later op een zeer prettige, professionele en ook informele manier samen aan deze studie zouden werken.

Zonder mijn studenten van de Masteropleiding Orthopedische Manuele Therapie en Psychosomatiek had ik de studies simpelweg niet zo goed kunnen uitvoeren. Jullie hebben keihard gewerkt, nauwkeurig geïncludeerd en jullie uiterste best gedaan om, zelfs na jullie studie, het aantal uitvallers tot een minimum te beperken. Bedankt!

Aan alle (oud-)collega's van het Lectoraat Leefstijl en Gezondheid – Sabine, Edwin, Stefan, Han, Francois, Janke, Sabine, Manon, Marike, Imke, Jacqueline N, Marleen, Eline, Barbara, Ryan, Richard, Annet, Henri, Jacqueline O en Mirjam – wat fijn was het om met jullie in zo'n warm en toegankelijk lectoraat te mogen werken. Jullie interesse, toegankelijkheid en betrokkenheid hebben een veilige haven gecreëerd waarin ik kon groeien. Onze peer-supportgroep was niet alleen gezellig, maar bood ook een waardevolle plek om met elkaar onze trajecten te bewandelen.

Naast de direct betrokkenen van mijn promotietraject, mijn promotieteam, co-auteurs, het lectoraat en studenten, zijn er ook heel veel collega's van het IBS en NVMT die betrokkenheid hebben getoond, mij hebben geïnspireerd en gestimuleerd gedurende dit promotietraject en ook in de fase daarvoor.

Ik prijs mij bijzonder gelukkig met alle collega's bij het IBS. Ons instituut is al bijna 15 jaar een plek waar ik mij enorm thuis voel en waar ik de kans heb gekregen

om mij professioneel te ontwikkelen. Dit is te danken aan collega's die persoonlijk geïnteresseerd zijn, elkaar op een positieve en kritische manier benaderen en die elkaar stimuleren en aanmoedigen om nieuwe dingen te ontdekken.

Een aantal belangrijke momenten in mijn (voor)traject wil ik graag benoemen: Kristel, Norman en Janke gaven mij het gevoel dat ik iemand zou kunnen zijn die een promotietraject kan aangaan en hebben zo het vonkje voor onderzoek in mij aangewakkerd. Jaap, als mijn leidinggevende, was direct enthousiast en heeft samen met mij alle mogelijkheden verkend om een promotietraject werkelijkheid te gaan maken. De eerste gesprekken met Harriët volgden daarna en het is dankzij de uitdagingen die het IBS mij bood dat ik het aandurfde deze weg in te slaan.

De ontwikkeling van *onze minor* samen met Allard, Jos, Fedde en Han was een bijzondere ervaring; we hebben enorm veel plezier gehad en veel geleerd van en met elkaar. Het was (en is) echt fijn samenwerken met jullie! Samen met het OMT-team hebben we veel ontwikkelingen doorgemaakt in de master, zoals het (her)ontwerpen van modules en lessen. Daar heb ik veel van geleerd, en dit alles heeft mij meer zelfvertrouwen gegeven.

Ik wil enkele collega's in het bijzonder noemen:

Selma, jouw oprechte interesse en kritische scherpzintheid waardeer ik enorm. Het is super om al zo lang met jou samen te werken (met als hoogtepunt natuurlijk Qatar!). Peter, jouw inspirerende manier van spreken over ons vak en de filosofische vragen die je stelt, brengen altijd plezier in de dag. Kristel, we zien elkaar de laatste tijd veel te weinig, maar de jaren bij de HU waren ook echt zo leuk dankzij jou. Niet alleen als collega, maar ook door onze vriendschap. Het samen trainen voor de marathon van Rotterdam en onze onvergetelijke reis naar Colombia en Panama zullen we nooit vergeten. Evelien, jouw betrokkenheid en warme persoonlijkheid zorgen altijd voor rust en relativering. Sophie, ik geniet van onze samenwerking en kijk ernaar uit om in de toekomst mooie projecten samen te doen. Eva, Nick en Marijn, ondanks dat we elkaar pas een paar jaar kennen, is ons contact ontzettend leuk. Ik kijk uit naar onze toekomstige fijne én gezellige samenwerking in zowel onderzoek als onderwijs.

Tijdens mijn promotietraject heb ik het geluk gehad om een aantal bijzondere congressen te bezoeken, dit waren ook echt hoogtepunten tijdens mijn promotietraject. Dankzij de HU kon ik hier naartoe en daar ben ik dankbaar voor. Naast dat deze congressen op professioneel vlak heel waardevol zijn geweest, heeft het

ook een enorme waarde voor de onderlinge contacten met collega's. Het congres in Groningen met Marijn, Mark en Eva zal ik nooit vergeten; we hebben elkaar beter leren kennen en we hebben ook gewoon een superleuke tijd gehad. Dit was niet minder met allemaal leuke collega's op het EFIC- en het IFOMPT-congres.

Ook wil ik het bestuur en de ambassadeurs van de NVMT noemen. Tijdens mijn promotietraject heb ik gezien hoe zij zich vol overgave inzetten voor ons prachtige vak. De activiteiten die ik als ambassadeur voor de NVMT heb mogen doen, waren niet alleen leerzaam, maar ook ontzettend leuk. Van Tom heb ik veel geleerd, vooral hoe hij ons vakgebied op een overkoepelende en bestuurlijke manier benadert. Daarnaast heb ik Roland leren kennen, een gepassioneerde en kritische onderzoeker. Jouw enthousiasme over de kleine stappen in mijn onderzoek heeft mij enorm gestimuleerd.

Naast de direct betrokkenen bij het promotietraject en fijne collega's zijn er voor mij ook een aantal heel belangrijke personen en vriendengroepen in mijn leven die van grote waarde zijn geweest tijdens mijn promotietraject.

Sabrine, inmiddels werken wij al 10 jaar heel intensief samen. We hebben bijna altijd op vrijdagen samen voor een groep masterstudenten gestaan. Binnen dit werk zijn wij $1 + 1 = 3$. Dat vinden wij zelf. Toen gingen we ook nog 'samen' een promotietraject starten. Ze zeggen wel eens dat je een promotietraject alleen doorloopt, voor mij is dat niet het geval. We zijn volledig samen opgetrokken in onze trajecten. Dat is zo ontzettend fijn geweest! Daarnaast ben je voor mij een hele belangrijke vriendin geworden; naast dat we veel lachen, kunnen we ook over alles praten. Je bent een prachtig mens.

Es, Inge en Cin, my Glorious Four, wij kennen elkaar al zo lang en ik vind het zo fijn dat we nog steeds *samen* zijn. We hebben zoveel met elkaar meegemaakt; een onverwoestbare vriendschap. Jullie leren mij om dingen in perspectief te zien en soms wat nuchterder naar het leven te kijken. Jullie zijn altijd betrokken geweest, hebben steeds gevraagd naar het proces en gecheckt of het niet te druk werd. Ik weet dat jullie er altijd voor mij zullen zijn en dat ben ik ook voor jullie. Ik ben echt zó blij met jullie!

Es, jij zult altijd mijn Jut of Jul blijven! Een groot deel van ons leven zijn we 'non-stop' samen geweest. Waar jij was, was ik en waar ik was, was jij. En als jij of ik op reis was, stuurden we gewoon eindeloos lange mailtjes naar elkaar. Dat is nu niet meer het geval, maar nog steeds leven we ons leven op een bepaalde manier

toch een beetje samen. Je betekent heel veel voor mij. Ik gun iedereen zo'n lieve, betrokken en goede vriendin als jij.

Mijn Mattiezzzz Es, Lin, Daan, Caro, Lau, Carlijn P, Carlijn V, Chris, Loes, Maaik, Marij; wat kan ik gelukkig zijn met zo'n fantastische, bijzondere en mooie vriendinnengroep. We staan al lang niet meer samen op het voetbalveld, maar gelukkig zien we elkaar nog heel regelmatig. De locaties zijn inmiddels wel wat veranderd: van ARC en de kroeg naar Ballorig, thuis met alle baby-mattiezzzz om ons heen, op wintersport met de snow-mattiezzzz of gewoon een weekendje met z'n allen naar Italië voor de onvergetelijke bruiloft van Lin en Daan. Bij ons maakt het eigenlijk niet zoveel uit wat iemand doet, zolang we maar blij zijn met wat we doen. En juist deze manier van omgaan met elkaar maakt mij gelukkig. Marij, superbedankt voor de extra Engelse lessen en het geven van feedback op mijn eerste stukken. Carlijn Prins, ondanks onze verschillende vakgebieden vond ik de overlappende aspecten in ons onderzoek en onze gesprekken daarover erg leuk en bijzonder waardevol. Bedankt voor wie jullie zijn, voor wie wij zijn en laten we dat nog heel lang zo houden.

Gabi und Wolfgang, ich möchte euch für die Zeit danken, die ihr mir und Michael gegeben habt, um gemeinsam schöne Dinge zu erleben oder um hart arbeiten zu können. Ihr kümmert Euch dann liebevoll um Jacob und Jolien, und die beiden finden das großartig! Sie genießen es mit euch zu spielen, zu bauen und zu basteln. Danke!

Ik ben opgegroeid in een warm en liefdevol gezin, samen met mijn zus en broer(tje). Een gezin dat elkaar niet alleen stimuleerde om te doen wat we echt leuk vonden, maar ook om alles met plezier en toewijding te doen. Zonder deze liefdevolle en stimulerende basis had ik mij misschien wel nooit aan een promotietraject gewaagd. Lieve papa en mama, jullie hebben altijd voor mij klaargestaan en dat doen jullie nog steeds. Ik ben daar intens dankbaar voor. En Marcella, wat ben ik gelukkig met een zus die ook nog eens zo'n goede vriendin is. Jij bent een van de belangrijkste mensen in mijn leven, iemand die mij mede heeft gevormd en altijd voor mij klaarstaat. Ik kan me geen betere zus wensen. Frank, jij hebt altijd op jouw eigengereide manier interesse getoond, vooral door het gesprek aan te gaan over wat wetenschap is en wanneer het relevant is voor de maatschappij. Dit heeft mij gestimuleerd om duidelijk te laten zien wat échte wetenschap is. Ondertussen zijn Mark en Marjolein als lieve zwager en schoonzus bij onze familie gekomen. Jullie hebben altijd betrokkenheid getoond. De manier hoe wij allemaal, met ook

alle kleintjes, Esmee, Jacob, Lot, Emily, Fijs en Jolien, met elkaar omgaan, is heel bijzonder en zo fijn.

Lieve Michael, zonder jouw support en vertrouwen had ik nooit de stap naar dit promotietraject gezet. Je hebt mij geholpen om mijn onzekerheden te overwinnen en moedigde mij aan om hard te werken, nauwkeurig te blijven, keuzes te maken en te relativieren. Jouw begrip over wat onderzoek en alles eromheen is, heeft mij enorm geholpen. Ik vind het heel fijn wat wij samen hebben en ben heel gelukkig. Samen genieten wij van twee prachtige kinderen en we bieden elkaar ruimte, de ruimte die we nodig hebben.

Lieve Jacob en Jolien, jullie zijn allebei geboren tijdens mijn promotietraject. Jullie aanwezigheid en vreugde gaven mij enorm veel positieve energie gedurende deze jaren. Zonder dat jullie het wisten, hielpen jullie mij om de nodige rust te nemen door simpelweg tijd met jullie door te brengen. De liefde en het geluk die jullie mij brengen, is niet in woorden te beschrijven.





About the author

Curriculum vitae

Martine Verwoerd, born in Leiderdorp on November 29, 1985, grew up in Alphen aan den Rijn with her parents, sister, and brother. She completed her higher secondary education in 2003 at Ashram College in Alphen aan den Rijn. She graduated with a bachelor in Physiotherapy degree cum laude from the University of Applied Sciences in Utrecht in 2007. Further, she completed her Professional Master's in Orthopaedic Manual Therapy with honors at the same institution in 2011. Since earning her bachelor's degree, she has worked in various primary care physiotherapy practices, primarily focusing on musculoskeletal disorders, with a special interest in spine-related problems. During the final year of her Master's program in 2011, she started working as a lecturer in the bachelor's program of Physiotherapy at Utrecht University of Applied Sciences and later in the Master's program in Orthopaedic Manual Therapy in 2015. Her collaboration with master's students led to her first publications in national journals. In 2018, a turning point in her career occurred when she was inspired to delve into scientific research, mentored and guided by Dr. Harriët Wittink. She officially began her PhD in the 'Lifestyle and Health' research group at Utrecht University of Applied Sciences, affiliated with the Care and Public Health Research Institute at Maastricht University, at the end of 2019. Between 2021 and 2023, she actively served as the Dutch Association for Manual Therapy (NVMT) ambassador. In 2024, she had the honor of giving the Rob Oostendorp Lecture for her contribution to the field of Manual Therapy. In 2019, Martine shifted her focus from clinical practice to a combination of teaching and research, while gratefully embracing her role as a mother to her son Jacob (born in 2019) and daughter Jolien (born in 2022).

List of publications

Publications in international peer-reviewed journals

Verwoerd MJ, Teunis MAT. Painr, An R data and analysis package, studying chronicity of neck pain in human patients. (v1.0.0). Zenodo; 2024. <https://doi.org/10.5281/zenodo.13744556>

Verwoerd MJ, Wittink H, Maissan F, Teunis M, Van Kuijk SMJ, Smeets RJEM. A prognostic model with an emphasis on modifiable factors to predict chronic pain after a new episode of acute- or subacute nonspecific idiopathic, non-traumatic neck pain presenting in primary care. *BMJ Open*. 2024;14:e086683. <http://doi.org/10.1136/bmjopen-2024-08668>

Verwoerd MJ, Wittink H, Maissan F, Van Kuijk SMJ, Smeets RJEM. A study protocol for the validation of a prognostic model with an emphasis on modifiable factors to predict chronic pain after a new episode of acute- or subacute nonspecific idiopathic, non-traumatic neck pain presenting in primary care. *PLoS One*. 2023;18(1):e0280278. <https://doi.org/10.1371/journal.pone.0280278>

Verwoerd MJ, Wittink H, Goossens MEJB, Maissan F, Smeets RJEM. Physiotherapists' knowledge, attitude and practice behavior to prevent chronification in patients with non-specific, non-traumatic, acute- and subacute neck pain: A qualitative study. *Musculoskelet Sci Pract*. 2022;57:102493. <http://doi.org/10.1016/j.msksp.2021.102493>

Verwoerd MJ, Wittink H, Maissan F, Smeets R. Consensus of potential modifiable prognostic factors for persistent pain after a first episode of nonspecific idiopathic, non-traumatic neck pain: results of nominal group and Delphi technique approach. *BMC Musculoskelet Disord*. 2020;21(1):656. <https://doi.org/10.1186/s12891-020-03682-8>

Verwoerd MJ, Wittink H, Maissan F, de Raaij E, Smeets RJEM. Prognostic factors for persistent pain after a first episode of nonspecific idiopathic, non-traumatic neck pain: A systematic review. *Musculoskelet Sci Pract*. 2019;42:13-37. <https://doi.org/10.1016/j.msksp.2019.03.009>

Verwoerd MJ, Wittink H, Maissan F, Teunis M, Van Kuijk SMJ, Smeets RJEM. Evaluating Clinical Characteristics and the Impact of Pain Severity on Functionality

and Emotional Well-Being in Non-Specific Neck Pain: A study in Primary Physiotherapy Care. Under review.

Pieterse T, Konings S, Stellato R, Boshuizen A, **Verwoerd MJ**. The construct validity of Brief Screenings Questions for Stress, Depression, Kinesiophobia and Catastrophizing in People With acute and subacute Neck Pain. In process.

Publications in national journals

Mourik P, **Verwoerd MJ**. In botsing met eigen waarden. Fysiopraxis. 2019.

Kooter H, **Verwoerd MJ**. Sportblessures vanuit een neuropathisch perspectief. Deel 1: werkingsmechanismen, diagnostiek en toepassing. Sportgericht. 2018;1.

Kooter H, **Verwoerd MJ**. Sportblessures vanuit een neuropathisch perspectief. Deel 2: werkingsmechanismen, interventies en toepassing. Sportgericht. 2018;3.

