BMJ Open

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Journal:	*BMJ Open*
Manuscript ID	bmjopen-2024-086683
Article Type:	Original research
Date Submitted by the Author:	22-Mar-2024
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Keywords:	REHABILITATION MEDICINE, Musculoskeletal disorders < ORTHOPAEDIC & TRAUMA SURGERY, PAIN MANAGEMENT, Prognosis

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Title

Development and internal validation of a multivariable prognostic model for chronification of non-specific neck pain in physiotherapy practice.

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Abstract

Objective: To develop and internally validate a prognostic model for the chronification of non-specific, non-traumatic neck pain in patients presenting to primary care physiotherapy, with an emphasis on modifiable psychosocial factors.

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

Setting: 30 primary care physiotherapy.

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

Baseline measures: Candidate prognostic variables were collected from participants regarding their neck pain symptoms, prior conditions, work-related factors, general factors, psychological and behavioral factors.

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 chronification of a (sub)acute non-specific neck pain and included mostly potentially modifiable factors for physiotherapy practice. External validation of this model is recommended.

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

Strengths and limitation of this study

- Novel approach to determine an accurate sample size for prognostic model development, mitigating overfitting.
- Inclusion of both biomedical and psychosocial prognostic factors which are potentially modifiable by a physiotherapist.
- Utilization of three follow-up time points for chronic pain outcome assessment.

Introduction

Neck pain is a widespread and disabling health condition significantly impacting public health.(1)(2)(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)

Physiotherapy is common first-line treatment; unfortunately, the effect is often only moderate.(7)(8)(9) Consequently, identifying prognostic factors for chronification of acute- and subacute neck pain is a top priority for neck pain research and for clinical care.(10) Understanding these factors can aid clinical decision making and potentially prevent the chronification of idiopathic neck pain.

The existing literature on prognostic models shows a low performance in predicting chronification of (sub)acute neck pain.(11) Moreover, the external validity of current prognostic models in terms of pain and recovery outcomes have not been proven in patients with (sub)acute neck pain.(12) 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 and > 3 months), clinical symptoms and prognosis. Additionally, much of the prognostic research has predominantly focused on non-modifiable factors, such as age, pain duration and sex, neglecting potentially modifiable factors.(11) 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 the chronification of pain.(13) Consequently, there is a compelling need for a biopsychosocial approach that specifically focuses on modifiable prognostic factors for chronification 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- or subacute neck pain, and (2) to develop and internally validate a model to predict chronification.

Methods

The methods of this study have been extensively described in the study protocol.(14) 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.(15)(16) This study adheres to the specific statistical recommendations for Type 3 prognostic model research.(15) The findings are reported according to the TRIPOD statement to ensure transparent reporting of the multivariable prediction model for individual prognosis (see Appendix 1).(16)

Study setting

Participants were recruited from 30 Dutch primary care physiotherapy 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.(17)

Participants

Patients were approached if they presented in one of the participating physiotherapy practices with a new episode of (sub)acute 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(18), widespread primary pain (ICD-11) (diffuse musculoskeletal pain in at least 4 of 5 body regions 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)(19), pain not caused by musculoskeletal origin (not located in the muscles, bones, joints, or tendons)(20), 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.(21)(14)

Candidate Prognostic factors

We included candidate prognostic for pain chronification, 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.(11)(22) Details on candidate prognostic factors and their measurement are provided in our study protocol.(11)

- **Patient characteristics**: sex and age.
- **Symptoms**: pain intensity at baseline measured with the NPRS, duration of the (sub)acute 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).(23)
- **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)(24)(22), and physical activity measured by meeting the activity level according to the Dutch Healthy Exercise Norm (Yes/No).(25)

- **Psychological and behavioral factors**: illness perceptions regarding recovery and pain identity, treatment beliefs, catastrophizing, depression and distress, kinesiophobia, coping, hypervigilance, and self-efficacy. Illness perceptions were assessed using the Dutch language version of the Brief Illness Perception Questionnaire (IPQ-DLV).(26) Catastrophizing was measured with the short version of the Pain Catastrophizing Scale (PCS).(27) To assess depression and distress, the 21-item version of the Depression Anxiety Stress Scale (DASS-21) was used.(28) Kinesiophobia was measured using the 11-item version of the Tampa Scale for Kinesiophobia (TSK).(29) Coping strategies were evaluated with the Pain Coping Inventory (PCI).(30)(31) Hypervigilance was assessed using the Pain Vigilance and Awareness Questionnaire (PVAQ)(32), and self-efficacy in managing pain was measured with the 2-item version of the Pain Self-Efficacy Questionnaire.(33)
- 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.(14)

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. 2019.(34) The expected value of the Cox-Snell R-squared of the new model was estimated at 0.23(35)(36)(22), and the estimated outcome event rate at 45%.(11) 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.(15) The Statistical software IBM SPSS (version 27) and R (version 4.2.2) were used for the statistical analysis.(37)(38) For the analysis, we extensively utilized the following R packages: tidyverse, MASS, pROC and Mice.(39)(40)(41)(42) The complete R script used in this study can be found on GitHub at https://github.com/uashogeschoolutrecht/painr (see Appendix 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). 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 a significant amount of missing data, which could not be imputed based on patient-specific information, resulting in the missing's remaining available for further analyses.

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 it's 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 ≥ 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 1). Among them, 62 participants (10%) developed chronic pain, while 541 participants experienced recovery from their pain.

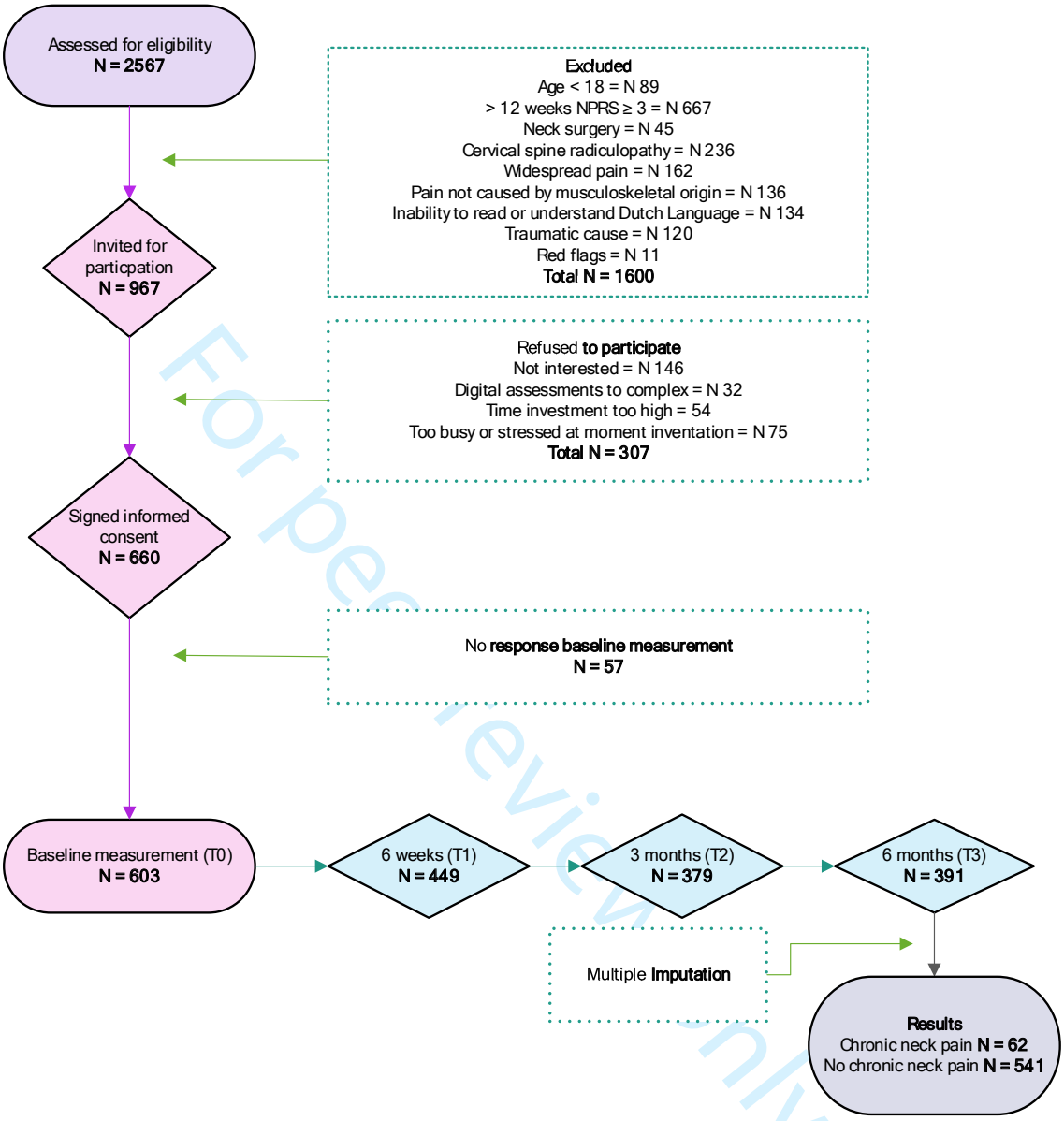

Figure 1. Flow-chart study

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 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.

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 increased to 224 at the 3-months follow-up, and to 231 at the 6-month mark.

	Number (percent)	Mean (SD) Median (IQR)	Missing Count (percent)
Patients characteristics			
Sex *1 = Male* *2 = Female*	 206 (34.2) 397 (65.8)		 0 (0)
Age		44,52 (15.7) 44,0 (31 - 56)	1 (.2)
Symptoms			
Pain intensity at baseline *(0-10)* *Higher scores indicate a higher degree of pain.*		5,93 (1.9) 6 (5 - 7)	0 (0)
Duration of neck pain *Number of weeks*		4.52 (2.9) 4 (2 - 6)	0 (0)
Recurrent pain *1 = No* *2 = Yes*	 198 (32.8) 404 (67)		1 (.2)
Reported pain in different body regions *1 = No* *2 = Yes*	 210 (34.8) 389 (64.5)		4 (.7)
Accompanying headache *1 = No* *2 = Yes* *3 = I had headache(s) before the neck pain.*	 247 (41) 281 (46.6) 70 (11.6)		5 (.8)
Disability (*0-7*) *Higher scores indicate higher interference of pain with daily activity. The sum score divided by the entered items.*		2.73 (2.1) 2.3 (1.0 – 4.1)	1 (.2)
Work related factors			
Work status 1 = Yes 2 = No	 501 (83.1) 92 (15.3)		10 (1.7)
Education 0 = Low level of education 1 = High level of eduction	 313 (51.9) 274 (45.4)		16 (2.7)
Happiness at work *1 = Happy (ref)* *2 = Neutral or not happy* *3 = Not working*	 376 (62.4) 112 (18.6) 92 (19)		23 (3.8)
Job satisfaction *1= Satisfied (ref)* *2 = Neutral or not satisfied* *3 = Not working*	 404 (67) 86 (14.3) 92 (18.7)		21 (3.5)
Potential to self-modify posture *1 = Possible (ref)* *2 = Neutral or impossible* *3 = Not working*	 372 (61.7) 114 (18.9) 92 (19.4)		25 (4.2)
General factors			
Physical activity *0 = Achieving the Dutch Healthy Exercise Norm* *1 = Not achieving the Dutch Healthy Exercise Norm*	 219 (36.3) 376 (62.3)		8 (1.3)

Smoking *1 = No* *2 = Yes*	 528 (87.6) 72 (11.9)		3 (.5)
Alcohol *1 = No* *2 = Yes*	 129 (21.4) 469 (77.8)		5 (.8)
BMI		25.31 (4,3) 24.66 (22.5 – 27.7)	
Sleep quality *0 = No negative experience with sleeping* *1 = Negative experience with sleeping*	 130 (21.6) 471 (78.1)		2 (.3)
Psychological and behavior factors			
Catastrophizing *(0–24)* Higher scores indicate more catastrophic thoughts		4.58 (4.6) 3 (1 – 7)	3 (.5)
Illness beliefs about recovery (Duration 0-10) *0 a very short time– 10 forever Higher scores indicate a maladaptive illness perception*		4.13 (2.7) 3 (2 – 6)	10 (1.7)
Illness beliefs about recovery (Concerned 0-10) *0 Not at all concerned– 10 extremely concerned Higher scores indicate a maladaptive illness perception.*		3.96 (2.6) 4 (2 – 6)	8 (1.3)
Treatment beliefs *(0–10)* *0 not at all—10 extremely helpful* *A lower score indicates a maladaptive illness perception*		7.82 (1.9) 8 (7 – 9)	12 (2.0)
Depression *(0–21)* *Higher scores indicate a higher degree of depression*		2.47 (3.3) 1 (0 – 4)	3 (.5)
Kinesiophobia *(11–44)* *Higher scores indicate a higher degree of kinesiophobia.*		16.5 (5.2) 15 (12 – 20)	3 (.5)
Distress *(0–21)* *Higher scores indicate a higher degree of stress.*		4.4 (4.1) 3 (1 – 7)	3 (.5)
Coping *0 = Passive coping* *1 = Active coping*	 120 (19.9) 478 (79.3)		5 (.8)
Illness beliefs about pain identity *(0–10)* *0 don't understand at all—10 understand very clearly. A lower score indicates a maladaptive illness perception.*		6.11 (2.3) 6 (5 – 8)	14 (2.3)
Hypervigilance *(0–80)* *Higher scores indicate a higher degree of vigilance.*		31.0 (11.4) 31 (23 – 38)	3 (.5)
Self-efficacy *(0–12)* *Higher scores indicate a higher degree of self-efficacy*		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* *2 = Biopsychosocial*	 134 (22.2) 420 (69.7)		49 (8.1)*

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

Table 1. Baseline characteristics of the study population

Univariable prognostic factors of development of chronic pain

The univariable analyses (see Figure 2) revealed significant positive associations between the following candidate prognostic factors and chronification of 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, increased 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.

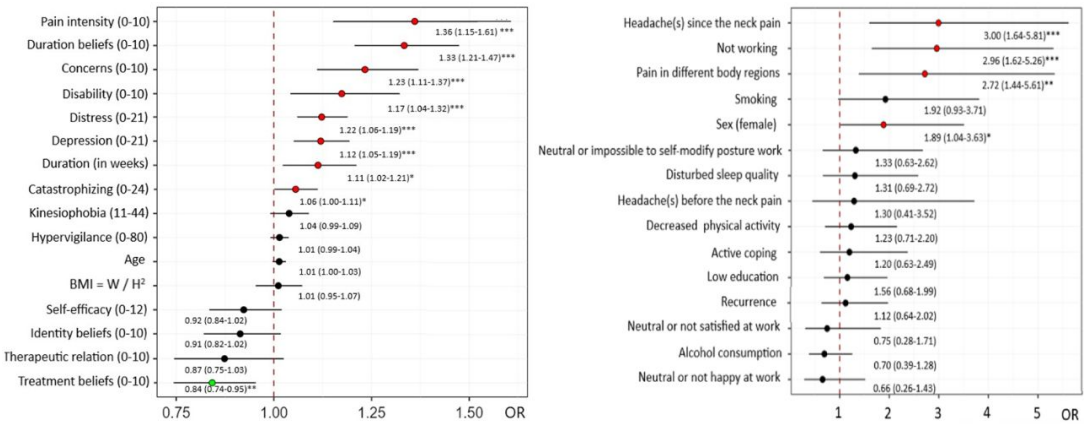

Figure 2. Univariable logistic regression analysis: unadjusted association between each candidate prognostic factor and the outcome chronic pain

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 $p \leq 0.001$.

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 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. The ORs including 95% confidence intervals are presented and visualized in Figure 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 4). The Hosmer-Lemeshow test yielded a p-value of 0.7167, indicating good model fit. The calibration plot (Figure 4) revealed acceptable to good calibration over the range of predicted probabilities. The Brier score was 0.077, indicating solid performance.

Internal validation prognostic model chronification neck pain

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 Table 2. The AUC after correction for optimism was 0.83. The optimism-corrected Nagelkerke's R^2 was 0.24.

The intermezzo section highlights a detailed patient profile to clarify the applicability and interpretation of our findings in a practical context. Supplemental figure presents an interactive visualization depicting the varied pain trajectories among participants within our cohort, alongside the linear predictor and the probabilities of chronification 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/. Additionally, an intermezzo

	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) *(reference)*			
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 *(reference)*	0.384	1.59 (0.71 - 3.43)	0.247
Neutral or impossible	1.311	4.87 (2.29 - 10.43)	<0.001 ***
Not working			
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

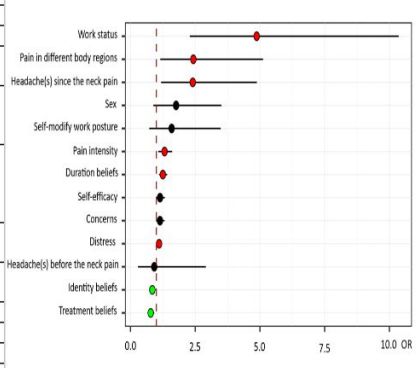

Figure 3 Adjusted multivariable logistic regression model

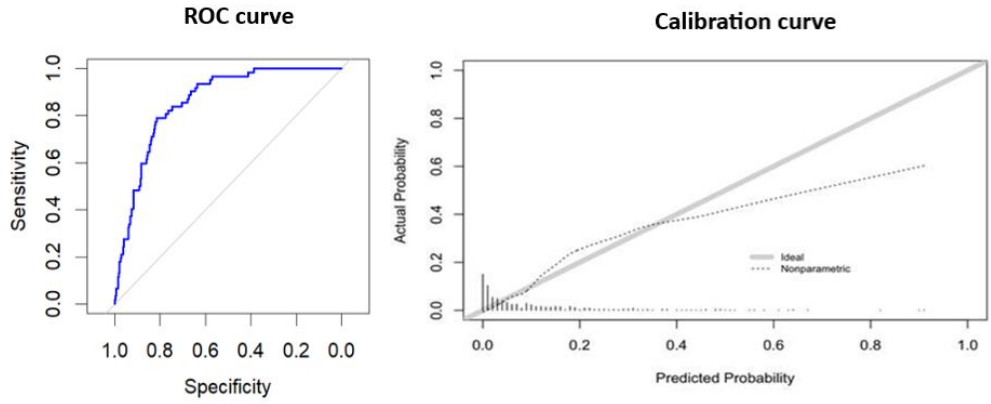

Figure 4. Area under the receiver operating characteristic and Calibration curve

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. Cur- rently, 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 under- standing 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.

Linear predictor (LP)

The linear predictor (LP) is given by:

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

+ (0.083 × distress)
−(0.142 × identity beliefs)
+ (0.109 × self-efficacy)

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 developed and internally validated a prognostic model for predicting the chronification of (sub) acute non-specific neck pain in patients presenting to primary care physiotherapy practices. The internal 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. We found several individual significant associations between non- and modifiable factors and the chronification of pain. The model comprising 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 headache, and employment status (not working). Potentially modifiable factors encompass baseline pain intensity, self-efficacy, headache onset concurrent with the 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 model with existing prognostic studies in musculoskeletal pain, several common factors emerge, including age, work status, reported pain in different body regions (headache included), baseline pain identity, and self-efficacy.(43)(44)(45)(46)(47) However, in our study, a higher score on the Pain Self-Efficacy Questionnaire 2-item version was associated with a higher odds of chronic neck pain. Notably, this association was characterized by a low regression coefficient and OR, and was also not significant with a small CI.

Our model incorporated four 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.(48)(49)(50) In prognostic multivariable models, the added prognostic value of illness perceptions varies.(50)(51) However, models developed and externally validated for neck pain often excluded illness beliefs from their set of candidate prognostic factors.(52)(53)(54)(11) Recent research has shown that modifying illness beliefs related to identity and concerns can mediate outcomes, specifically disability and pain, within primary care physiotherapy practices.(55) 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.(56)(13) These factors did not retain 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.(56) 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.(57)(58)(59)(60)(61) In contrast, it is important to note that the majority of studies involving patients with (sub)acute musculoskeletal have primarily focused on pain and disability as outcomes, rather than exploring changes in psychological factors as moderators or as outcome variables.(62)(63)(64)

Nevertheless, it remains important for primary care physiotherapists to feel competent and capable of effectively addressing these psychological factors and illness beliefs. Unfortunately, the integration of the biopsychosocial model into the primary care physiotherapeutic management of musculoskeletal disorders has to date not been entirely successful.(65)(66)

The incidence of chronic pain in our participants 6 months after first presentation at a physiotherapist with (sub)acute non-specific and non-traumatic neck pain differed from our systematic review findings. In our preliminary sample size calculation, a 45% chronicity rate for neck pain was assumed. This rate was calculated by dividing the number of patients by the number of non-recovery of pain cases.(11) This disparity can be attributed to our definition of chronic pain and measurement approach. Unlike the single time point follow-up assessments (e.g. 3, 6, or 12 months) with a specific pain score threshold used in most studies(67), including those in our review(11), our study used a more comprehensive method. We assessed pain intensity at 6 weeks, 3 months, and 6 months post-baseline, requiring NPRS score of ≥ 3 at each time point to classify them as having chronic pain.(14) This approach provides a more precise representation of chronic pain as a continuous experience. By using this methodology, we excluded the recurrent pain group with pain-free or mild time periods, diverging from the International Classification of Diseased 11th Revision (ICD-11) broader definition of chronic pain that includes recurrent pain.(19) We hypothesize that differentiating between continuous and recurrent pain will lead to a more effective prognostic model, acknowledging the distinct pain experiences of these groups.

The ICD-11 characterizes chronic primary musculoskeletal pain as a disease that is accompanied by significant emotional distress (such as anxiety, anger/frustration, or depressed mood) or functional disability, which includes interference with daily life activities and reduced participation in social roles. This delineation underpins the rationale for distinguishing between mild and moderate pain, with a proposed threshold of ≥ 3 to define the latter category. This distinction is based on the observation that mild pain typically does not entail marked emotional distress or functional

disability.(68)(69) However, literature indicates that establishing a definitive cut-off point for mild and moderate pain, particularly in terms of pain-related interference with functioning and emotions, is complex.(69)(70)(71)

The ICD-11 further recommends the assessment of patient-reported pain using an 11-point scale, focusing on pain intensity and its interference with psychological and physical functioning in daily life for both research purposes and a comprehensive understanding of the patient's pain experience.(19) Nevertheless, for the purposes of comparison and updating various prognostic models, the adoption of a standardized international threshold for chronic pain is recommended.

Limitations

The calibration curve suggests substantial overestimation of higher risks; this estimation was based on only a few patients, as most had a relatively low estimated risk of chronification. This potential overestimation is, nevertheless, unlikely to remain visible in an external validation with enough participants at high risk.

In the initial sample size calculation, we assumed a 45% incidence of chronic pain, based on our systematic review.(11) This calculation allowed for 26 candidate prognostic variables among a cohort of 598 participants.(34) However, this study yielded a lower-than-expected incidence of chronic pain, with only 10% of participants, indicting 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 1.

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 an individual patient's probability of experiencing chronic neck pain. Furthermore, it can be beneficial to assess and

intervene on the modifiable factors in our model. 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 NSNP (TRIPOD statement).(16)

Conclusion

This model has the potential to obtain a valid prognosis for chronification of non-specific neck pain and included 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 Applies 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.

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Appendix 1. TRIPOD Checklist Prediction Model Development and Validation

Section/Topic	ı	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
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
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Limitations	18	Discuss any limitations of the study (such as nonrepresentative sample, few events per predictor, missing data).	28
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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

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Link Github:
https://github.com/uashogeschoolutrecht/painr

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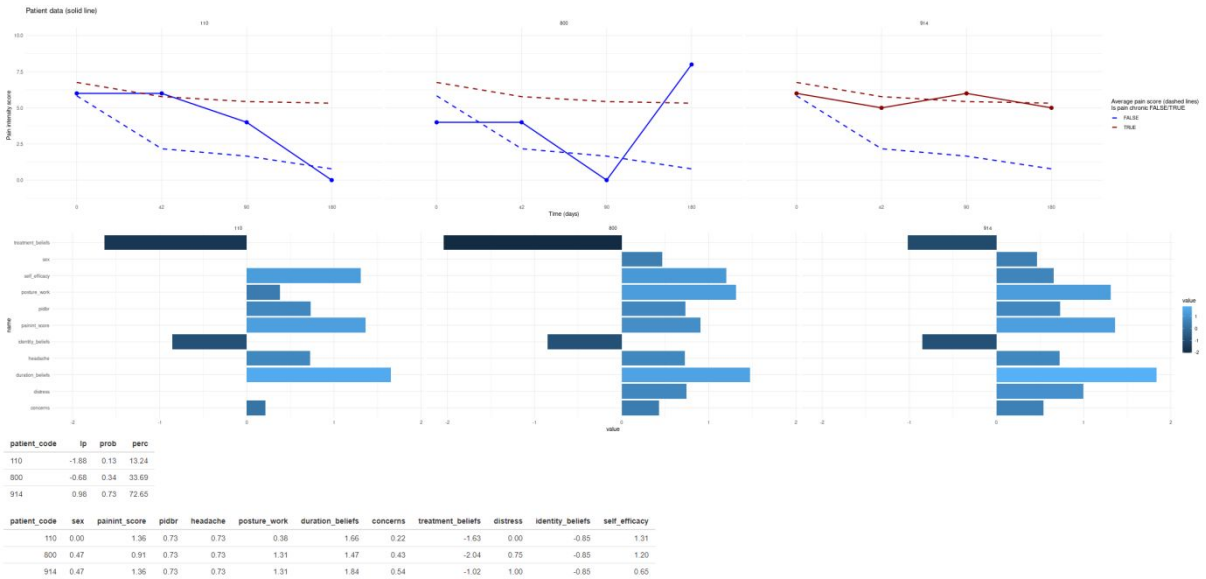
Supplemental Figure



patient_code	lp	prob	perc
110	-1.88	0.13	13.24
800	-0.68	0.34	33.69
914	0.98	0.73	72.65

patient_code	sex	painint_score	pidbr	headache	posture_work	duration_beliefs	concerns	treatment_beliefs	distress	identity_beliefs	self_efficacy
110	0.00	1.36	0.73	0.73	0.38	1.66	0.22	-1.63	0.00	-0.85	1.31
800	0.47	0.91	0.73	0.73	1.31	1.47	0.43	-2.04	0.75	-0.85	1.20
914	0.47	1.36	0.73	0.73	1.31	1.84	0.54	-1.02	1.00	-0.85	0.65

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. "LP" stands for linear predictor, "Prob" represents the probability of chronicity, and "Perc" indicates the percentual 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.

TRIPOD Checklist Prediction Model Development and Validation

Development and internal validation of a multivariable prognostic model for chronification of non-specific neck pain in physiotherapy practice.

Section/Topic		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
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
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BMJ Open

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Journal:	*BMJ Open*
Manuscript ID	bmjopen-2024-086683.R1
Article Type:	Original research
Date Submitted by the Author:	11-Jul-2024
Complete List of Authors:	Verwoerd, Martine; HU University of Applied Sciences Utrecht, Institute of Movement Studies Wittink, Harriët ; HU University of Applied Sciences Utrecht Maissan, Francois ; HU University of Applied Sciences Utrecht, Movement studies Teunis, Marc; HU University of Applied Sciences Utrecht van Kuijk, Sander; Maastricht Universitair Medisch Centrum+, Clinical Epidemiology and Medical Technology Assessment Smeets, Rob; Maastricht University, Rehabilitation medicine; CIR, Revalidatie
Primary Subject Heading:	Evidence based practice
Secondary Subject Heading:	Mental health
Keywords:	REHABILITATION MEDICINE, Musculoskeletal disorders < ORTHOPAEDIC & TRAUMA SURGERY, PAIN MANAGEMENT, Prognosis

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Title

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.

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Abstract

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 behavioural 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

Strengths and limitations of this study

- Novel approach to determine an accurate sample size for prognostic model development, mitigating overfitting.
- Inclusion of biomedical, psychological, and social prognostic factors which are potentially modifiable by a physiotherapist.
- Utilization of three follow-up time points for chronic pain outcome assessment.

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 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)

Patient and public involvement statement

None

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 food) 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.

2019.(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 2 the table of contents).(44)

We used multiple imputation with fully conditional specification to impute incomplete records, assuming data to be at least missing at random (MAR).(45) 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 it's 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 ≥ 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 1). Among them, 62 participants (10%) developed chronic pain, while 541 participants experienced recovery from their pain.

For the description of the participants' characteristics, including candidate prognostic factors, and the number of participants with missing data, see Table 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.

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.(45)

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 3.

	Number (percent)	Mean (SD) Median (IQR)	Missing Count (percent)
Patients characteristics			
Sex *1 = Male* *2 = Female*	 206 (34.2) 397 (65.8)		 0 (0)
Age		44,5 (15.7) 44,0 (31 - 56)	1 (.2)
Symptoms			
Pain intensity at baseline *(0-10)* *Higher scores indicate a higher degree of pain.*		5,9 (1.9) 6 (5 - 7)	0 (0)
Duration of neck pain *Number of weeks*		4.5 (2.9) 4 (2 - 6)	0 (0)
Recurrent pain *1 = No* *2 = Yes*	 198 (32.8) 404 (67)		1 (.2)
Reported pain in different body regions *1 = No* *2 = Yes*	 210 (34.8) 389 (64.5)		4 (.7)
Accompanying headache *1 = No* *2 = Yes* *3 = I had headache(s) before the neck pain.*	 247 (41) 281 (46.6) 70 (11.6)		5 (.8)
Disability (*0-7*) *Higher scores indicate higher interference of pain with daily activity. The sum score divided by the entered items.*		2.73 (2.1) 2.3 (1.0 – 4.1)	1 (.2)
Work related factors			
Work status 1 = Yes 2 = No	 501 (83.1) 92 (15.3)		10 (1.7)
Education 0 = Low level of education 1 = High level of eduction	 313 (51.9) 274 (45.4)		16 (2.7)
Happiness at work *1 = Happy (ref)* *2 = Neutral or not happy* *3 = Not working*	 376 (62.4) 112 (18.6) 92 (19)		23 (3.8)
Job satisfaction *1= Satisfied (ref)* *2 = Neutral or not satisfied* *3 = Not working*	 404 (67) 86 (14.3) 92 (18.7)		21 (3.5)
Potential to self-modify posture *1 = Possible (ref)* *2 = Neutral or impossible* *3 = Not working*	 372 (61.7) 114 (18.9) 92 (19.4)		25 (4.2)
General factors			
Physical activity *0 = Achieving the Dutch Healthy Exercise Norm* *1 = Not achieving the Dutch Healthy Exercise Norm*	 219 (36.3) 376 (62.3)		8 (1.3)

Smoking *1 = No* *2 = Yes*	 528 (87.6) 72 (11.9)		3 (.5)
Alcohol *1 = No* *2 = Yes*	 129 (21.4) 469 (77.8)		5 (.8)
BMI		25.31 (4.3) 24.66 (22.5 – 27.7)	
Sleep quality *0 = No negative experience with sleeping* *1 = Negative experience with sleeping*	 130 (21.6) 471 (78.1)		2 (.3)
Psychological and behavior factors			
Catastrophizing *(0–24)* Higher scores indicate more catastrophic thoughts		4.58 (4.6) 3 (1 – 7)	3 (.5)
Illness beliefs about recovery (Duration 0-10) *0 a very short time– 10 forever Higher scores indicate a maladaptive illness perception*		4.13 (2.7) 3 (2 – 6)	10 (1.7)
Illness beliefs about recovery (Concerned 0-10) *0 Not at all concerned– 10 extremely concerned Higher scores indicate a maladaptive illness perception.*		3.96 (2.6) 4 (2 – 6)	8 (1.3)
Treatment beliefs *(0–10)* *0 not at all—10 extremely helpful* *A lower score indicates a maladaptive illness perception*		7.82 (1.9) 8 (7 – 9)	12 (2.0)
Depression *(0–21)* *Higher scores indicate a higher degree of depression*		2.47 (3.3) 1 (0 – 4)	3 (.5)
Kinesiophobia *(11–44)* *Higher scores indicate a higher degree of kinesiophobia.*		16.5 (5.2) 15 (12 – 20)	3 (.5)
Distress *(0–21)* *Higher scores indicate a higher degree of stress.*		4.4 (4.1) 3 (1 – 7)	3 (.5)
Coping *0 = Passive coping* *1 = Active coping*	 120 (19.9) 478 (79.3)		5 (.8)
Illness beliefs about pain identity *(0–10)* *0 don't understand at all—10 understand very clearly. A lower score indicates a maladaptive illness perception.*		6.11 (2.3) 6 (5 – 8)	14 (2.3)
Hypervigilance *(0–80)* *Higher scores indicate a higher degree of vigilance.*		31.0 (11.4) 31 (23 – 38)	3 (.5)
Self-efficacy *(0–12)* *Higher scores indicate a higher degree of self-efficacy*		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* *2 = Biopsychosocial*	 134 (22.2) 420 (69.7)		49 (8.1)*

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

Table 1. Baseline characteristics of the study population

Univariable prognostic factors of development of chronic pain

The univariable analyses (see Figure 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.

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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 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 4). The Hosmer-Lemeshow test yielded a p-value of 0.7167, indicating good model fit. The calibration plot (Figure 4) revealed acceptable to good calibration over the range of predicted probabilities. The Brier score was 0.077, indicating solid performance.

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 3. The AUC after correction for optimism was 0.83. The optimism-corrected Nagelkerke's R^2 was 0.24.

The intermezzo section highlights a detailed patient profile to clarify the applicability and interpretation of our findings in a practical context. Supplemental figure 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.

Linear predictor (LP)

The linear predictor (LP) is given by:

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

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.(46–50) 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.(51,52) 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.(53) This notable outcome might, therefore, be questioned.

Our model incorporated four 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.(54–56) However, in prognostic multivariable models, the contribution of illness perceptions to the robustness of a prognostic model varies.(56,57) Notably, illness beliefs are often excluded from the candidate prognostic factors in models developed and externally validated for neck pain models.(12,58–60) 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.(61) 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.(14,62) 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.(63) 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.(50,63–65) 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.(50,66,67)

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(68), 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 Diseased 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.(69,70) 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.(70–72) 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 subjectively using a non-validated question, which poses a limitation as it may not

distinguish between perceived and actual behavior during 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 are changing their positions. Additionally, this type of questioning prevents us from confirming the accuracy of reports, such as whether a patient who claims they cannot change positions is indeed unable to do so. Establishing the validity and discriminative ability of the different concepts being tested is important to investigate.

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 is the guarantor, 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 Applies 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.

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Figure legend:

Figure 1 - Flow-chart study

Table 1 - Baseline characteristics of the study population

Figure 2 - Univariable logistic regression analysis: unadjusted association between each candidate prognostic factor and the outcome of chronic pain

Figure 3 - Adjusted multivariable logistic regression model

Figure 4 – Area under the receiver operating characteristic and calibration curve

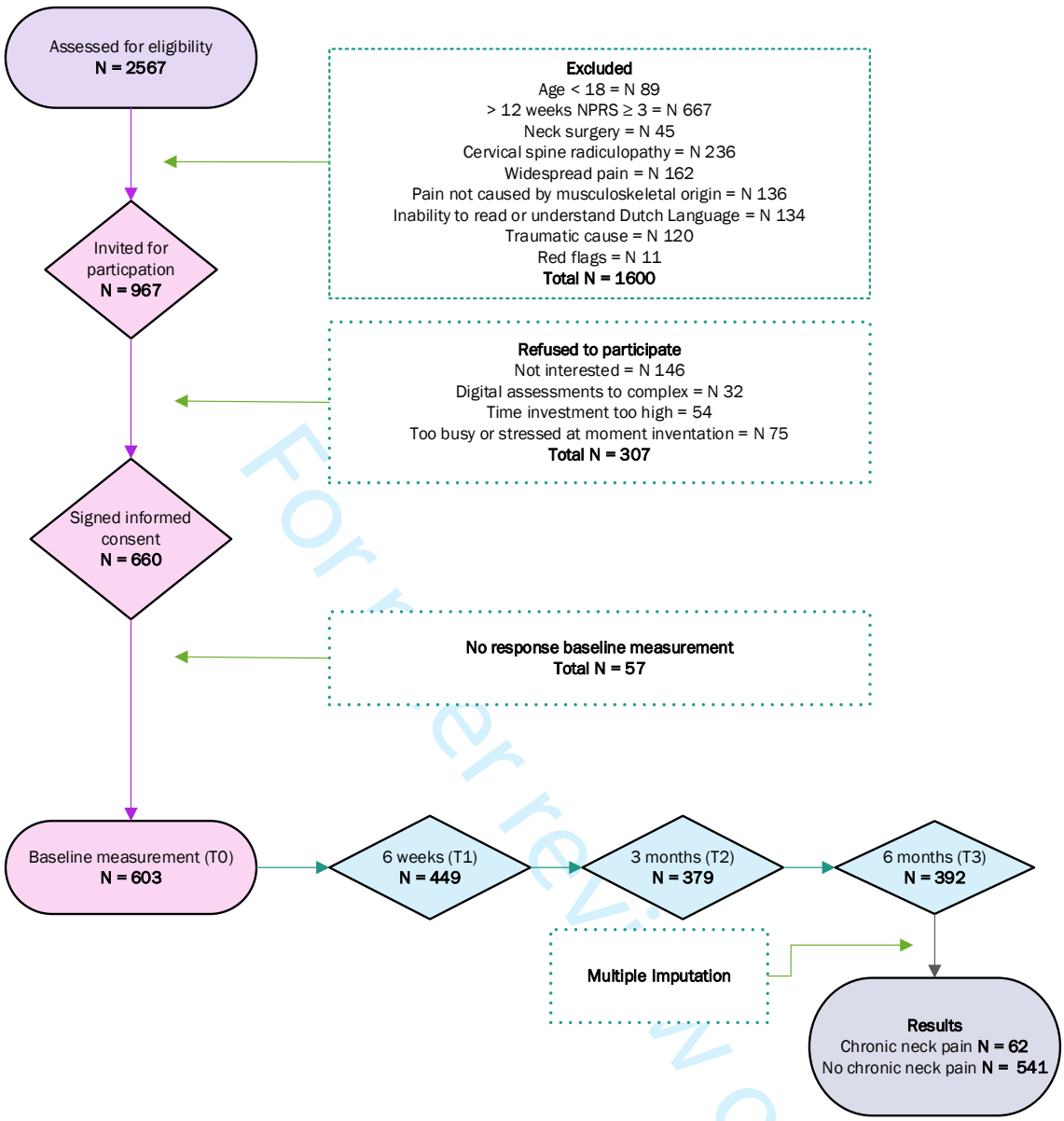


Figure 1. Flow-chart study

N = Number, T = Time-point

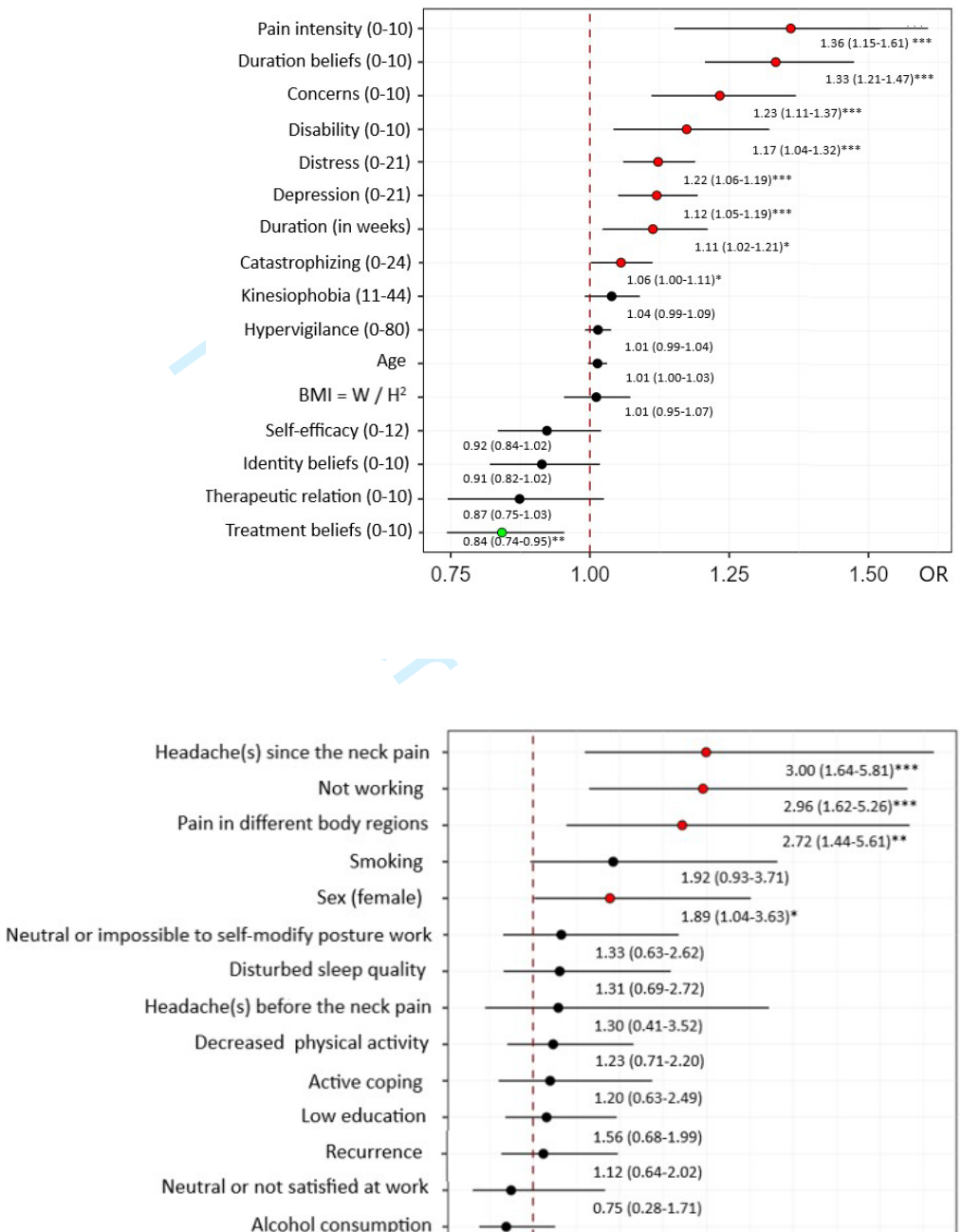


Figure 2. Univariable logistic regression analysis: unadjusted association between each candidate prognostic factor and the outcome of chronic pain

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) *(reference)*			
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 *(reference)*	0.384	1.59 (0.71 - 3.43)	0.247
Neutral or impossible	1.311	4.87 (2.29 - 10.43)	<0.001 ***
Not working			
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

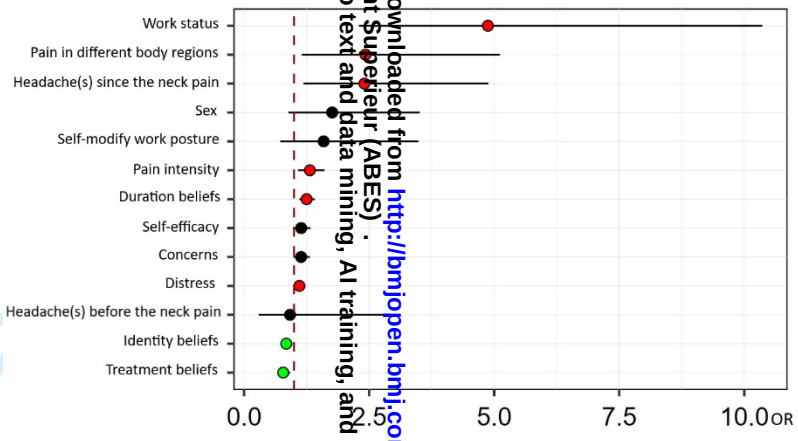


Figure 3 Adjusted multivariable logistic regression model

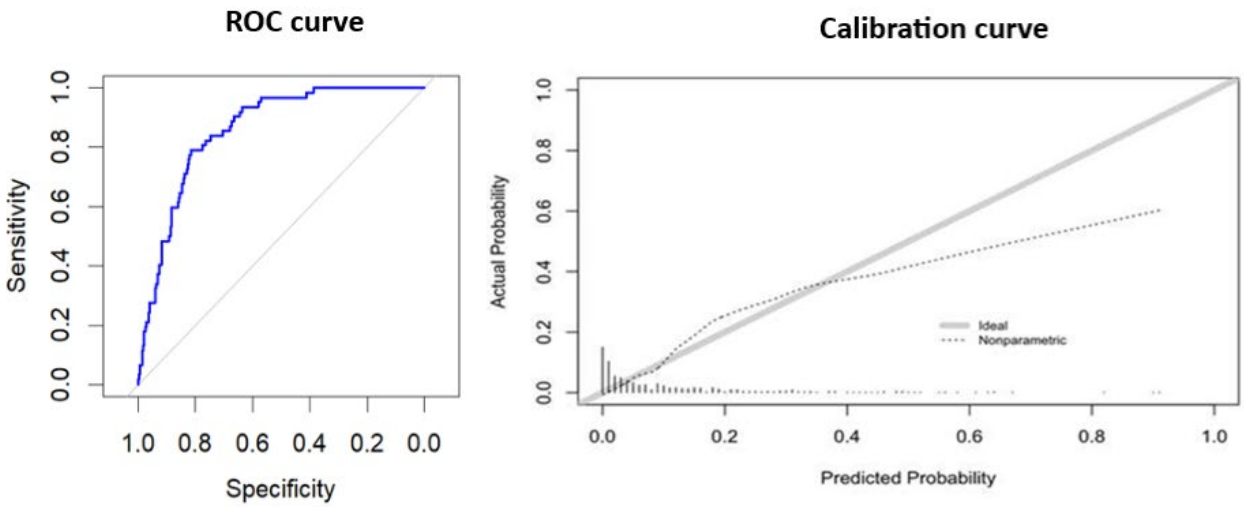


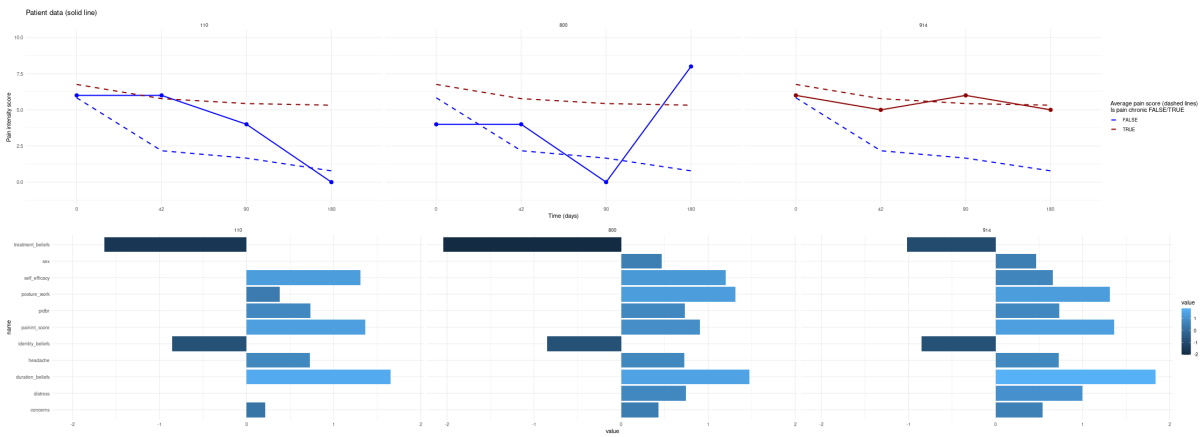
Figure 4. Area under the receiver operating characteristic and Calibration curve

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.

Supplementary Information

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. "LP" stands for linear predictor, "Prob" represents the probability of chronicity, and "Perc" indicates the percentual 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.



patient_code	lp	prob	perc
110	-1.88	0.13	13.24
800	-0.68	0.34	33.69
914	0.98	0.73	72.65

patient_code	sex	painint_score	pidbr	headache	posture_work	duration_beliefs	concerns	treatment_beliefs	distress	identity_beliefs	self_efficacy
110	0.00	1.36	0.73	0.73	0.38	1.66	0.22	-1.63	0.00	-0.85	1.31
800	0.47	0.91	0.73	0.73	1.31	1.47	0.43	-2.04	0.75	-0.85	1.20
914	0.47	1.36	0.73	0.73	1.31	1.84	0.54	-1.02	1.00	-0.85	0.65

Supplementary Information

Appendix 1. TRIPOD Checklist Prediction Model Development and Validation

Section/Topic	ı	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
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
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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

Supplementary Information

Appendix 2 Table of contents

Link Github:

https://github.com/uashogeschoolutrecht/painr

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3.11 Get individual lines for each patient
3.12 Write to disk as excelfile 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

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5. Article figures

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5.22 Formally testing the Goodness-of-fit using the Hosmer and Lemeshow

5.23 Intermezzo – linear predictors

Supplementary Information

Appendix 3 Overview Applied interventions study population

Table 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

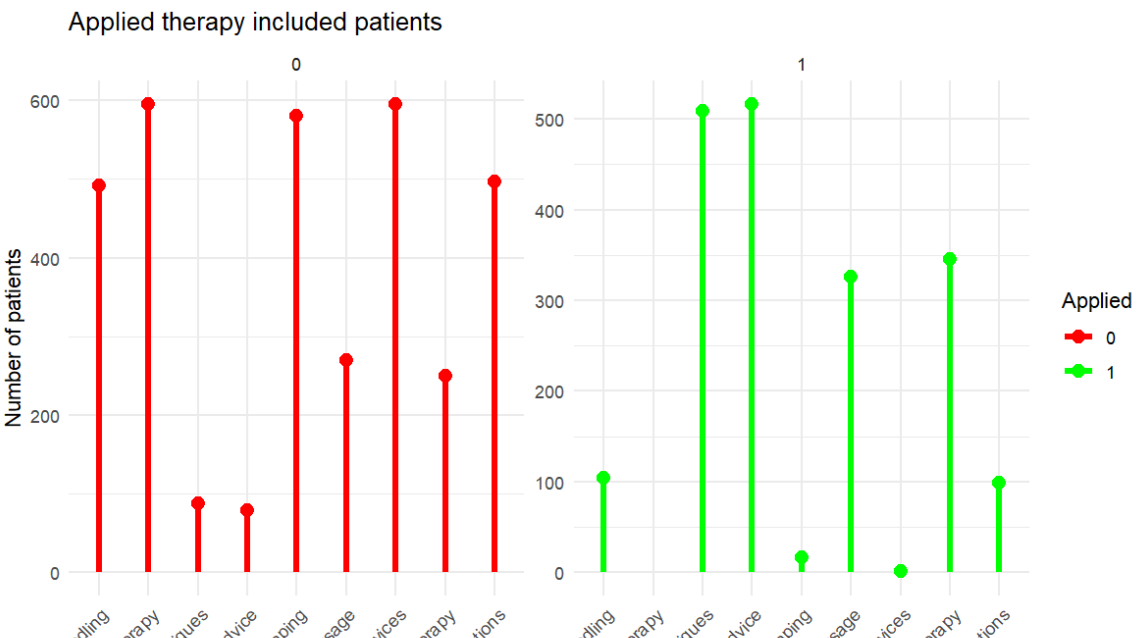

Figure: Applied therapy included patients (N = 596)

TRIPOD Checklist Prediction Model Development and Validation

Development and internal validation of a multivariable prognostic model for chronification of non-specific neck pain in physiotherapy practice.

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