BMJ Open

BMJ Open is committed to open peer review. As part of this commitment we make the peer review history of every article we publish publicly available.

When an article is published we post the peer reviewers' comments and the authors' responses online. We also post the versions of the paper that were used during peer review. These are the versions that the peer review comments apply to.

The versions of the paper that follow are the versions that were submitted during the peer review process. They are not the versions of record or the final published versions. They should not be cited or distributed as the published version of this manuscript.

BMJ Open is an open access journal and the full, final, typeset and author-corrected version of record of the manuscript is available on our site with no access controls, subscription charges or pay-per-view fees (http://bmjopen.bmj.com).

If you have any questions on BMJ Open's open peer review process please email info.bmjopen@bmj.com

BMJ Open: first published as 10.1136/bmjopen-2018-024557 on 24 April 2019. Downloaded from http://bmjopen.bmj.com/ on May 15, 2025 at Department GEZ-LTA Erasmushogeschool . Protected by copyright, including for uses related to text and data mining, AI training, and similar technologies.

BMJ Open

Predictive models for short- and long-term improvement in women under physiotherapy for chronic disabling neck pain

Journal:	*BMJ Open*
Manuscript ID	bmjopen-2018-024557
Article Type:	Research
Date Submitted by the Author:	04-Jun-2018
Complete List of Authors:	Bohman, Tony; Karolinska Institutet, Dep. of Neurobiology, Care Sciences and Society; Karolinska Institutet, Institute of Environmental Medicine Bottai, Matteo; Karolinska Institutet, Institue of Environmental Medicine Björklund, Martin; University of Gävle, Department of Occupational and Public Health Sciences; Umeå University, Department of Community Medicine and Rehabilitation
Keywords:	prediction, prognosis, non-specific neck pain, longitudinal analyses, cohort, clinical important improvement

SCHOLARONE™
Manuscripts

For peer review only

BMJ Open: first published as 10.1136/bmjopen-2018-024557 on 24 April 2019. Downloaded from http://bmjopen.bmj.com/ on May 15, 2025 at Department GEZ-LTA Erasmushogeschool . Protected by copyright, including for uses related to text and data mining, AI training, and similar technologies.

Predictive models for short- and long-term improvement in women under physiotherapy for chronic disabling neck pain

Tony Bohman, PhD[1,2], Matteo Bottai, ScD[3], Martin Björklund, PhD[4,5]

[1] Department of Neurobiology, Care Sciences and Society, Division of Physiotherapy, Karolinska Institutet, 23 100, SE-14183, Stockholm, Sweden, [2] Unit of Cardiovascular Epidemiology, Institute of Environmental Medicine, Karolinska Institutet, Box 210, SE-17177, Stockholm, Sweden, [3] Unit of Biostatistics, Institute of Environmental Medicine, Karolinska Institutet, Box 210, SE-17177, Stockholm, Sweden, [4] Department of Occupational and Public Health Sciences, Centre for Musculoskeletal Research, University of Gävle, Gävle, Sweden, [5] Department of Community Medicine and Rehabilitation, Umeå University, Umeå, Sweden

Corresponding author:

Tony Bohman, Department of Neurobiology, Care Sciences and Society, Karolinska Institutet, 23 100, SE-14183, Stockholm, Sweden

e-mail; tony.bohman@ki.se, cellphone; +46 70 299 62 63

Key words; prediction, prognosis, non-specific neck pain, neck pain, longitudinal analyses, cohort, clinical important improvement, discrimination

Word count: 3980

Figures: 1

Tables: 4

References: 47

Supplementary files: 0

For peer review only

BMJ Open: first published as 10.1136/bmjopen-2018-024557 on 24 April 2019. Downloaded from http://bmjopen.bmj.com/ on May 15, 2025 at Department GEZ-LTA Erasmushogeschool . Protected by copyright, including for uses related to text and data mining, AI training, and similar technologies.

For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

ABSTRACT

Objectives

To develop predictive models for short- and long-term clinically important improvement in women with non-specific chronic disabling neck pain during the clinical course of physiotherapy.

Design

Longitudinal cohort study based on data from a randomized controlled trial evaluating short- and long-term effects on sensorimotor function, over eleven weeks of physiotherapy.

Participants and settings

Eighty-nine women aged 31-65 years with non-specific chronic disabling neck pain from Gävle, Sweden.

Measures

The outcome, clinically important improvement, was measured with the Patient Global Impression of Change Scale (PGICS) and the Neck Disability Index (NDI), assessed by self-administered questionnaires at 3, 9 and 15 months from the start of the interventions (baseline). Eleven baseline prognostic factors were considered in the analyses. The predictive models were built using general estimation equations. The sensitivity and specificity of the models were measured by the area under the receiver operating characteristic curve (AUC). Internal validity was estimated by using statistical bootstrapping.

Results

Prognostic factors of short- and long-term improvement in the final models were: neck disability and recovery expectations for the PGICS outcome, and neck disability, depression and catastrophizing for the NDI outcome. Some prognostic factors could predict different short- and long-term outcomes, as did catastrophizing in the NDI model. Internal validation showed estimated AUC of 0.67 (95% CI;

For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

BMJ Open: first published as 10.1136/bmjopen-2018-024557 on 24 April 2019. Downloaded from http://bmjopen.bmj.com/ on May 15, 2025 at Department GEZ-LTA Erasmushogeschool . Protected by copyright, including for uses related to text and data mining, AI training, and similar technologies.

0.59-0.75) and 0.67 (95% CI; 0.58-0.76) for PGICS and NDI, respectively, indicating acceptable predictive ability.

Conclusion

The predictive models evaluating clinical important improvement from chronic non-specific neck pain among women in the clinical course of physiotherapy included different sets of prognostic factors for the two outcomes considered. The effect of prognostic factors may vary over time. The predictive models for both outcomes showed acceptable sensitivity and specificity. Before using them in clinical practice, however, these models should be validated in other populations and tested in clinical settings.

Article summary

Strengths and limitations of this study

- Strengths of this study are a well-defined sample and the thorough development of predictive models.
- Moreover, the longitudinal design with a short- and long follow-up time, and the inclusion of biopsychosocial prognostic factors in the analyses further strengthens the study.
- Possible limitations of this study include the relatively small sample.

For peer review only

BMJ Open: first published as 10.1136/bmjopen-2018-024557 on 24 April 2019. Downloaded from http://bmjopen.bmj.com/ on May 15, 2025 at Department GEZ-LTA Erasmushogeschool . Protected by copyright, including for uses related to text and data mining, AI training, and similar technologies.

For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

BMJ Open: first published as 10.1136/bmjopen-2018-024557 on 24 April 2019. Downloaded from http://bmjopen.bmj.com/ on May 15, 2025 at Department GEZ-LTA Erasmushogeschool . Protected by copyright, including for uses related to text and data mining, AI training, and similar technologies.

INTRODUCTION

Neck pain is a very common health problem and a cause of substantial disability, social and economic impact throughout the world.[1] The prevalence of neck pain has increased during the last decades, and in 2015, neck pain together with low back pain, were the leading causes of disability.[2] Hoy et al. found the 2010 global age-standardised point prevalence of neck pain to be 4.9% with the highest overall prevalence in North America (6.5%) and western Europe (6.3%).[3] Hogg-Johnson et al. reported the 12-month prevalence of neck pain to range between 30% and 50% and the 12-month prevalence of activity-limiting pain to be 1.7% to 11.5% with a higher prevalence among women.[1] Most often persons affected by neck pain have pain without specific pathology.[4] Although neck pain generally has a favourable course, neck pain is likely recurrent and may become chronic.[5 6] In a review from 2008 Carroll et al. concluded that 50% to 85% of persons with neck pain do not experience complete resolution of their pain.[5]

Prognostic research can help understand the course and future outcome in individuals with neck pain.[7] Guzman et al. summarised the work of the 2000-2010 Neck Pain Task Force concluding that younger age, no previous pain, good physiological and psychological health, good coping, good social support, exercise and sports, and no prior sick leave may increase the chance of recovery from neck pain.[8] Walton et al. surveyed prognostic factors for prolonged recovery from neck pain in 13 systematic reviews.[9] They found evidence only for past history of musculoskeletal disorders and older age to prolong recovery in non-whiplash related neck pain. For the remaining factors evaluated there was insufficient evidence for the influence on neck pain, and more research was requested.

Neck pain patients commonly seek physical therapy and predicting treatment outcome and prognosis for these patients is challenging.[10] To meet this challenge, predictive models including multiple prognostic factors could guide health care providers such as physiotherapists in how to predict which patients are more likely to improve and to help patients with neck pain manage their expectations.[11 12] Such models are recommended to be developed in well-defined context with respect to patient population and the healthcare provided.[11] Women have a higher risk of chronic neck pain, and it has been suggested that women should be assessed separately from men in prognostic research.[13-15] Using

For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

a search strategy for predictive models in physiotherapy and musculoskeletal complaints, suggested by van Oort et al., we found only one study by Cecchi et al. using a chronic population, and none with a model specific for women.[16 17]

Considering the recurrent course of neck pain the predictive value of potential prognostic factors may change over time following physiotherapy.[17 18] Longitudinal analyses would be a proper method to evaluate these potential changes over time as such analyses accounts for the correlation and time dependency between follow-up measures, and has been recommended for use in prospective cohort studies on musculoskeletal problems.[19 20] The present study aimed to, with the use of longitudinal analyses, develop predictive models for short- and long-term clinically important improvement in women with chronic disabling neck pain in the clinical course of physiotherapy.

METHODS

Design and study population

This longitudinal cohort study sought to develop predictive models, including multiple prognostic factors jointly, for chronic neck pain in women. Predictive models are one of the four themes of the Prognosis Research Strategy Framework for Prognostic Studies.[7 12] Carroll et al. classify predictive models as "Phase II" studies in a 3-level hierarchy of evidence from longitudinal studies, and suggests them suitable for predicting recovery from neck pain.[5]

We used data from a randomized control trial (RCT) evaluating the short- and long-term effects, following eleven weeks of physiotherapy interventions (coordination exercise, strength training and massage), on sensorimotor function in 108 women with non-specific chronic disabling neck pain.[21] The trial was carried out in Gävle, Sweden, in 2008 and was approved by the ethics review board in Uppsala, Sweden. Participants gave their written consent to participate in the RCT.

Eligible for the RCT were Swedish-speaking women aged 25 to 65 years with non-specific disabling neck pain lasting for 3 months or more (chronic). The women were recruited via the social insurance agency and by advertisement in local papers and invitations at municipality and county council work

For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

BMJ Open: first published as 10.1136/bmjopen-2018-024557 on 24 April 2019. Downloaded from http://bmjopen.bmj.com/ on May 15, 2025 at Department GEZ-LTA Erasmushogeschool . Protected by copyright, including for uses related to text and data mining, AI training, and similar technologies.

sites, primary and occupational healthcare units. Non-specific chronic disabling neck pain was defined as pain drawing of the "most painful area" together with reported disability measured as more than 9 normalised points of the first 19 items in the Disability Arm Shoulder Hand questionnaire (DASH).[22 23] These 19 items refer to disability in activities of daily living regarding neck, shoulders and arms. Excluded were individuals with trauma to the head or neck, a diagnosis of rheumatic, neurological, connective tissue, inflammatory or endocrine disease or psychiatric diagnosis affecting their everyday life. Also excluded were those with fibromyalgia, cancer, stroke, cardiac infarction, diabetes type I, cervical radiculopathy, vestibular disorders, surgery or fracture to the back, neck, or shoulder in the last 3 years or shoulder luxation in the last year, and if they had performed strenuous exercise more than 3 times per week during the previous 6 months.[21]

Patient and Public Involvement

As this study was based on secondary data from a RCT, patients were not directly involved in the design and completion of the study.

Data collection and variables

Before start of the intervention (baseline) participants filled in a self-administered questionnaire, containing instruments and questions to measure the potential prognostic factors. Outcome information was collected by follow-up questionnaires at three, nine and 15 months from baseline. Participants without outcome information from none of the three follow-ups were excluded resulting in a study population of 89 participants (Figure 1).

Figure 1

Outcome

Patient Global Impression of Change Scale (PGICS) provided information for the outcome "global perceived change of general health" by comparing general health at follow-up with general health at baseline. PGICS is a 7-point ordinal Likert scale (very much improved, much improved, minimally improved, not changed, minimally worse, much worse and very much worse).[24] The scale categories were dichotomized into "improved" (very much improved, much improved) and "not improved" (all

For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

BMJ Open: first published as 10.1136/bmjopen-2018-024557 on 24 April 2019. Downloaded from http://bmjopen.bmj.com/ on May 15, 2025 at Department GEZ-LTA Erasmushogeschool . Protected by copyright, including for uses related to text and data mining, AI training, and similar technologies.

the other categories). According to the IMMPACT recommendations for clinical important outcomes in chronic pain the 7- point scale is recommended when assessing general health, and the category "very much improved" and "much improved" reflects what patients consider to be an important change in general health.[25] The Neck Disability Index (NDI) provided information for the second outcome.[26] The NDI has 10 items (pain intensity, personal care, lifting, reading, headaches, concentration, work, driving, sleeping and recreational activities) with 6 possible answers in each item, scored 0 (no limitation) to 5 (major limitations). Total score of the NDI range from 0 to 50. The NDI has high reliability, strong internal consistency and strong validity compared to other instruments for evaluating patients with neck pain.[26] In the present study we used the normalized NDI (NDI %, 0-100). A minimal important change (MIC) for the NDI % was set to 6.3.[27] Using MIC as a cut-off, a dichotomized NDI outcome was constructed for each follow-up where "improved" was equal to a NDI % decrease of more than 6.3 between the baseline and the follow-up and "not improved" was equal to a decrease no larger than 6.3 or an increase. Participants with a NDI % of 0 at follow-up were also defined as "improved" no matter the baseline score.

Potential prognostic factors

The selection of potential prognostic factors was based on systematic reviews and prospective studies on the prognosis of non-specific neck pain, clinical considerations and availability in the data (Table 1).[5 9 28 29]

For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

BMJ Open: first published as 10.1136/bmjopen-2018-024557 on 24 April 2019. Downloaded from http://bmjopen.bmj.com/ on May 15, 2025 at Department GEZ-LTA Erasmushogeschool . Protected by copyright, including for uses related to text and data mining, AI training, and similar technologies.

Table 1. Potential prognostic factors and corresponding references.

Potential prognostic factors	Measurement	Categorisation in the analyses
Age	Age at baseline	Continuous
Neck disability[26]	Normalised Neck Disability Index (NDI%)	Continuous, 1-100 0 = "no disability" and 100 = "complete disability"
Average pain intensity[39]	Average pain intensity during the previous week measured on an 11-point Numeric Rating Scale (NRS)	Continuous, 0-10 0 = "no pain" and 10 = "pain as bad as it could be"
Depression[40]	Self-rating version of the Montgomery Åsberg Depression Rating Scale (MADRS-S)	Continuous, 0-54 0 = "no depressive symptoms" and 54 = "severe depression"
Fear of movement[41 42]	The Tampa scale of kinesiophobia	Continuous, 17-68 A sum score of 17-68 were higher score indicate higher fear of movement
Catastrophizing[43]	The six item catastrophizing subscale from the Coping Strategies Questionnaire (CSQ).	Continuous, 0-36 Each item of the subscale had a score of 0-6 were a high score indicated a high degree of catastrophizing
Social support[44]	Item number 5 and 14 of the Swedish Multidimensional Pain Inventory (MPI-S)	Continuous, 1-12 Each item with a score of 0-6, where 0 = "no social support" and 12 = "high social support"

For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

BMJ Open: first published as 10.1136/bmjopen-2018-024557 on 24 April 2019. Downloaded from http://bmjopen.bmj.com/ on May 15, 2025 at Department GEZ-LTA Erasmushogeschool .

Protected by copyright, including for uses related to text and data mining, AI training, and similar technologies.

Recovery expectation[33]	The answer to the question; "Do you think that any intervention or exercise will lead to recovery?"	Continuous, 1-5 5 point ordinal Likert scale from 1 = "No, definitely not" to 5 = "Yes, completely recovered"
Chronic widespread pain[6 45]	Derived from a pain drawing	Yes; pain in all 4 quadrants of the body together with spinal pain
Leisure physical activity[46]	"How much have you, in general, moved or exerted yourself physically during leisure time in the past year"	- No/low intensity; very little/an occasional walk or similar/ every day physical activity like gardening, cleaning/low intensity physical activity e.g. walking or similar at least once a week - Moderate/high intensity; more strenuous physical activity e.g. jogging, swimming etc. at least once a week/regular high intensity physical activity e.g. running, ball sports etc.
Physical workload[47]	"How physically strenuous has your work or daily activity been the past 12 months?"	- Mostly sedentary - Low/heavy work load; low physical work load but mobile/quite physically strenuous work/physically strenuous work
Dual-working	A combination of three items; 1) Working/not working. 2) What does your household look like?	- Yes; 1) working, 2) living together with children and/or another adult person and 3) having the responsibility for the housework - No; any other combination of the three items (see

For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml
BMJ Open: first published as 10.1136/bmjopen-2018-024557 on 24 April 2019. Downloaded from http://bmjopen.bmj.com/ on May 15, 2025 at Department GEZ-LTA Erasmushogeschool . Protected by copyright, including for uses related to text and data mining, AI training, and similar technologies.

	3) Who is primarily responsible for and performing the housework in your family?	the method section)

For peer review only

BMJ Open: first published as 10.1136/bmjopen-2018-024557 on 24 April 2019. Downloaded from http://bmjopen.bmj.com/ on May 15, 2025 at Department GEZ-LTA Erasmushogeschool . Protected by copyright, including for uses related to text and data mining, AI training, and similar technologies.

For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

Average pain intensity was not limited to neck pain but all participants had reported neck pain as their "most painful area" as this was a criterion for inclusion in the RCT.[21] Dual-working was a combination of three items: 1) Working/not working, 2) What does your household look like? (living alone, living alone with children, living with another adult, living with another adult and children), 3) Who is primarily performing the housework in your family? (myself, someone else, equally shared). The factor dual-working was then dichotomized according to the answers into; yes (working, living with children and/or another adult, and performing the housework) and no (any other combination of the three items). Dual-working has to our knowledge not been evaluated in previous studies, but is to our opinion possibly associated to the prognosis of neck pain in women.

Statistical methods

Descriptive statistics were presented by median and interquartile range (IQR). The level of the confidence intervals (CI) was set at 95% and that of the tests at 5%. All p-values were two-sided. Stata version 14.2 (StataCorp College Station, TX, USA) was used in the analyses.

General Estimation Equations (GEE) with a logit link, a Bernoulli family, and an exchangeable working correlation structure, were used to estimate the probability of a clinically important improvement of the outcomes from baseline to three and 15-months follow-up visits.[19] Data from all three follow-ups were used in the analyses. GEE can model this type of longitudinal data efficiently, while taking into account the potential dependence of the repeated measures taken on each participant.[19] To check for within-group dependence of data we used logistic regression analyses of the association between the dichotomized outcome measures, PGICS and NDI respectively, at the three, nine and 15-month follow-ups, separately. Both outcomes showed strong associations between the follow-ups which indicated that GEE was required in the subsequent analyses. The analyses were done separately for each of the two outcome measures, PGICS and NDI, and were based on complete data sets. Associations were expressed as population-average odds ratios (OR) along with 95% CI.

The linearity of the relationship between the logit of the probability of the outcome variable and the numeric independent variable was verified by means of restricted cubic splines.[19 30 31] We found evidence against the assumption of linearity when neck disability was the independent variable and

For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

BMJ Open: first published as 10.1136/bmjopen-2018-024557 on 24 April 2019. Downloaded from http://bmjopen.bmj.com/ on May 15, 2025 at Department GEZ-LTA Erasmushogeschool . Protected by copyright, including for uses related to text and data mining, AI training, and similar technologies.

PGICS the outcome measure. Therefore, the restricted cubic splines for neck disability were used in the further analyses.[19]

Univariate analyses

GEE were used for all potential prognostic factors one at a time to estimate the time-specific OR for each of the two outcome measures separately. When the analyses showed an OR independent of time, i.e. the effect measure modification as measured by the interaction term (factor-by-time) was not statistically significant, the analyses were repeated without the effect measure modification. This resulted in a single OR showing the population average OR for the factor from three to 15 months. When effect measure modification was present the OR at three and 15 months were reported separately. Potential prognostic factors with a p-value ≤ 0.2 for the estimated OR were considered as candidate factors for the multivariable analyses.[31] Based on an à priori decision of clinical relevance statistical effect measure modifications were tested between pain intensity and depression or recovery expectations. The effect measure modification, if found statistically significant, was included in further analyses.[32]

Developing the models

A sequential backward manual selection procedure based on the GEE regression was used to build the predictive models.[31]All candidate factors were included in the initial multivariable model. The factor with the highest p-value (Wald-test) were excluded one by one until all factors in the model had a p-value ≤ 0.1.[31] If a candidate factor showed effect measure modification with time, then the factor was included together with the effect measure modification in the multivariable model. If the analysis showed signs of collinearity the factor judged most clinically relevant was kept in the model. The association between the prognostic factor and the outcome was reported as beta-coefficient (β) with standard error (SE), OR with 95% CI and associated p-value.

Evaluation of the models

The bias corrected area under the receiver operating characteristic curve (AUC) with 95% CI was obtained by cross validation based on 100 design-matrix bootstrap replicates and used to determine

For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

BMJ Open: first published as 10.1136/bmjopen-2018-024557 on 24 April 2019. Downloaded from http://bmjopen.bmj.com/ on May 15, 2025 at Department GEZ-LTA Erasmushogeschool . Protected by copyright, including for uses related to text and data mining, AI training, and similar technologies.

the internally validated predictive ability of the models.[32] The AUC represents the ability of the model to distinguish between participants that will or will not improve during the follow-up period. The AUC ranges from 0.5 (no predictive ability) to 1.0 (perfect predictive ability).

Sensitivity analyses

To compare the study population with non-responders we used the chi-squared and Fisher's exact test for categorical variables, and the t-test or the Wilcoxon test for continuous variables.

RESULTS

Study population

Baseline characteristics of the study population are listed in Table 2. At baseline the women's age ranged between 31 and 65 years, and all women reported neck pain duration of more than eight months. Eighty women (91%) were working and 66 (74%) reported no sick leave due to neck pain during the previous 6 months. Using PGICS as outcome measure 47 (53%) participants were categorised as improved at 3-month and 26 (30%) at 15-month follow-up while using NDI as outcome measure 39 (44%) women had improved at 3 months and 31 (36%) at 15 months.

Table 2. Baseline characteristics of the study population, (*n=89*).

Characteristics		Missing (n)[a]
Age median (IQR)	52 (47-59)	0
Neck disability median (IQR)	28 (20-33)	0
Average pain intensity median (IQR)	5 (4-6)	0
Depression median (IQR)	8 (6-12)	1
Fear of movement median (IQR)	29 (26-33)	0
Catastrophizing median (IQR)	6 (3-11)	0
Social support median (IQR)	6 (4-9)	1
Recovery expectation median (IQR)	4 (3-4)	4

For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

BMJ Open: first published as 10.1136/bmjopen-2018-024557 on 24 April 2019. Downloaded from http://bmjopen.bmj.com/ on May 15, 2025 at Department GEZ-LTA Erasmushogeschool . Protected by copyright, including for uses related to text and data mining, AI training, and similar technologies.

Chronic widespread pain freq (%)		0
Yes	40 (45)	
Leisure physical activity freq (%)		0
No/low intensity	60 (67)	
Moderate/high intensity	29 (33)	
Physical workload freq (%)		1
Mostly sedentary	36 (41)	
Low/heavy work load	52 (59)	
Dual-working freq (%)		4
Yes	38 (45)	

[a] missing answer, IQR; interquartile range, freq; frequency

Development and evaluation of the predictive model

The univariate analyses are presented in Table 3. The follow-up data observations used for the analyses differed slightly between the two outcome measures due to missing responses (Figure 1). There was no effect measure modification found between pain intensity and depression or recovery expectations. In the univariate analyses with PGICS as outcome measure age, neck disability, average pain intensity and recovery expectations met the inclusion criteria for the multivariable analysis. No potential prognostic factor showed effect measure modification with time. The corresponding analyses with NDI as outcome measure yielded five potential prognostic factors that met the criteria for the multivariable analysis: age, neck disability, depression, catastrophizing and leisure physical activity. Catastrophizing showed time dependency why an effect measure modification term (catastrophizing x time) were added to the multivariable analysis.

For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

BMJ Open: first published as 10.1136/bmjopen-2018-024557 on 24 April 2019. Downloaded from http://bmjopen.bmj.com/ on May 15, 2025 at Department GEZ-LTA Erasmushogeschool . Protected by copyright, including for uses related to text and data mining, AI training, and similar technologies.

Table 3. Univariate GEE analyses for short- and long-term potential prognostic factors with PGICS and NDI as outcome. Study population *n=89*.

Potential prognostic factors included in the development of the multivariable predictive models are presented with an asterisk (*).

Potential prognostic factor	PGICS			Potential prognostic factor	NDI		
	n/obs[a]	OR 3-15 m (p)[b]	p-eff.m.[c]		*n/obs*[a]	OR 3–15m (p)[b]	p-eff.m.[c]
Age*	*89/263*	0.96 (0.09)	0.76	**Age***	89/262	0.97 (0.20)	0.68
Neck disability*	*89/263*			**Neck disability***	89/262	1.04 (0.02)	0.30
NDI 16 to 28[d]		0.96 (0.35)	0.69	**Average pain intensity**	89/262	1.10 (0.37)	0.69
NDI 28 to 42[e]		1.11 (0.05)	0.89	**Depression***	88/259	0.96 (0.17)	0.71
Average pain intensity*	*89/263*	1.26 (0.05)	0.88	**Fear of movement**	89/262	1.00 (0.85)	0.86
Depression	*88/260*	1.02 (0.54)	0.05	**Catastrophizing***	89/262		0.02
Fear of movement	*89/263*	0.99 (0.71)	0.46	OR 3 m (p-value)[f]		1.06 (0.10)	
Catastrophizing	*89/263*	1.03 (0.34)	0.20	OR 15 m (p-value)[g]		0.96 (0.24)	
Social support	*88/260*	1.04 (0.44)	0.64	**Social support**	88/259	1.05 (0.34)	0.73
Recovery expectations*	*85/253*	1.33 (0.20)	0.32	**Recovery expectations**	85/253	0.82 (0.32)	0.38
Chronic widespread pain	*89/263*		0.36	**Chronic widespread pain**	89/262		0.08
No		1.0		No		1.0	
Yes		1.33 (0.43)		Yes		0.79 (0.49)	

For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml
BMJ Open: first published as 10.1136/bmjopen-2018-024557 on 24 April 2019. Downloaded from http://bmjopen.bmj.com/ on May 15, 2025 at Department GEZ-LTA Erasmushogeschool . Protected by copyright, including for uses related to text and data mining, AI training, and similar technologies.

Leisure physical activity	*89/263*		0.44	**Leisure physical activity***	89/262		0.36
No/low intensity		1.0		No/low intensity		1.0	
Moderate/high intensity		0.88 (0.73)		Moderate/high intensity		0.63 (0.20)	
Physical workload	*88/260*		0.56	**Physical workload**	88/259		0.06
Mostly sedentary		1.0		Mostly sedentary		1.0	
Low to heavy workload		1.15 (0.71)		Low to heavy workload		1.07 (0.85)	
Dual-working	*85/251*		0.44	**Dual-working**	85/250		0.18
No		1.0		No		1.0	
Yes		0.90 (0.77)		Yes		0.68 (0.25)	

OR= odds ratio, an OR>1 reflects an higher odds of clinical important improvement and an OR<1 reflects an lower odds of clinical important improvement.

PGICS: Patient Global Impression of Change Scale; 1=improved/0=not improved, NDI: normalized Neck Disability Index; 1=improved/0=not improved, [a]number of participants in the analyses/number of outcome observations in the analyses, [b]population average odds ratios for clinically important improvement between 3 to 15 months, [c]p-value for the effect modification over time between 3 to 15 months from baseline, [d and e]Neck disability index (NDI%) analysed as cubic splines, [f and g]population average odds ratios for clinically important improvement at 3 and 15 months respectively.

For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

BMJ Open: first published as 10.1136/bmjopen-2018-024557 on 24 April 2019. Downloaded from http://bmjopen.bmj.com/ on May 15, 2025 at Department GEZ-LTA Erasmushogeschool .

Protected by copyright, including for uses related to text and data mining, AI training, and similar technologies.

The resulting predictive models from the sequential selection procedure are presented in Table 4. There were no signs of collinearity in the multivariable analyses. Internal validation showed robust models with a predictive ability of 0.67 for both outcomes (Table 4).

For peer review only

For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

BMJ Open: first published as 10.1136/bmjopen-2018-024557 on 24 April 2019. Downloaded from http://bmjopen.bmj.com/ on May 15, 2025 at Department GEZ-LTA Erasmushogeschool . Protected by copyright, including for uses related to text and data mining, AI training, and similar technologies.

Table 4. The final predictive models as a result from the multivariable GEE analyses of clinically important improvement in chronic disabling neck pain with PGICS and NDI as outcomes.

Prognostic factors	**PGICS *(85/253)*[a]**			**Prognostic factors**	**NDI *(88/259)*[a]**		
	β (SE)	**OR (95% CI)**	**p-value**		**β (SE)**	**OR (95% CI)**	**p-value**
Neck disability				**Neck disability**	0.05 (0.02)	1.05 (1.02, 1.09)	<0.01
NDI 16 to 28[b]	-0.05 (0.04)	0.95 (0.88, 1.04)	0.26	**Depression**	-0.08 (0.03)	0.92 (0.86, 0.98)	0.01
NDI 28 to 42[c]	0.12 (0.05)	1.12 (1.02, 1.24)	0.02	**Catastrophizing**			
Recovery expectations	0.50 (0.23)	1.65 (1.04, 2.61)	0.03	3 months	0.05 (0.04)	1.05 (0.98, 1.14)	0.18
				15 months	-0.06 (0.04)	0.95 (0.88, 1.02)	0.17
				x time[d]	-0.01 (0.00†)	0.99 (0.98, 1.00‡)	0.02
AUC (95% CI)[e]	0.67 (0.58, 0.76)			**AUC (95% CI)[e]**	0.67 (0.59, 0.75)		

OR=odds ratio, an OR>1 reflects a higher odds of clinical important improvement and an OR<1 reflects a lower odds of clinical important improvement, β=beta coefficient, SE=standard error, PGICS: Patient Global Impression of Change Scale; 1=improved/0=not improved, NDI: normalized Neck Disability Index; 1=improved/0=not improved, [a] number of participants in the analysis/number of outcome observations in the analysis, [b and c] Neck disability index (NDI%) analysed as restricted cubic splines, [d] effect measure modification term in the model; catastrophizing x time, [e] internally validated receiver operating characteristics curve (AUC) with 95% CI, † 0.0040, ‡ 0.9988.

For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

BMJ Open: first published as 10.1136/bmjopen-2018-024557 on 24 April 2019. Downloaded from http://bmjopen.bmj.com/ on May 15, 2025 at Department GEZ-LTA Erasmushogeschool . Protected by copyright, including for uses related to text and data mining, AI training, and similar technologies.

Sensitivity analyses

Non-responders (n=19) showed no statistically significant differences in the characteristics compared to the study population except for average pain intensity where non-responders had a higher median of 6.5 compared to a median of 5 (p = 0.03) in the study population.

DISCUSSION

We have developed and internally validated predictive models for clinically important short- and long-term improvement from chronic disabling neck pain among women in the clinical course of physiotherapy. The outcome was assessed using "global perceived change of general health" (PGICS) and the Neck Disability Index (NDI) in the two models, respectively. Both models were robust and had acceptable predictive ability.[32] The results showed that, when assessing potential biopsychosocial prognostic factors, perceived disabilities related to neck pain, depression, catastrophizing and recovery expectations are of importance for predicting short- and long-term improvements in these women. Further, we found that prognostic factors could predict different results depending on the follow up time, as for catastrophizing in the model with NDI as outcome, something important to notice in the management of these patients. Similar to previous studies, we found that the prognostic factors in the models could differ depending on the outcome.[18 33]

Our results indicate that the population-average odds for clinically important improvement, with PGICS as outcome measure, increase with higher levels of disability related to neck pain, and the higher expectations of recovery the women reported at baseline. With NDI as a outcome measure, the odds for improvement increased with higher levels of neck pain-related disability and decrease with higher levels of depression. These results were valid over the total follow up time of 15 months. However, the model with NDI as outcome indicated increased odds for short-term improvement, but decreased odds for long-term improvement the higher the levels of catastrophizing at baseline. This interesting finding was made possible by the longitudinal nature of our study design. To the best of our knowledge, this is the first study using longitudinal analyses in predictive models for neck pain.

For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

BMJ Open: first published as 10.1136/bmjopen-2018-024557 on 24 April 2019. Downloaded from http://bmjopen.bmj.com/ on May 15, 2025 at Department GEZ-LTA Erasmushogeschool . Protected by copyright, including for uses related to text and data mining, AI training, and similar technologies.

Interestingly, depression was found to be a predictor even though women with a psychiatric diagnosis affecting their everyday life were excluded from the study population which resulted in low baseline levels of depression.

The relative strength of the incorporated factors in the model should be interpreted with great caution as their independent effect on the outcome was not thoroughly examined.

After comparing our findings to other similar studies we concluded that the results are diverse, probably due to different populations, potential prognostic factors examined, outcomes and follow up times. As earlier mentioned, we found only one prediction study on patients with chronic non-specific neck pain in physiotherapy, but with a study population also including males.[17] The authors found poor outcome at discharge and one year from discharge from physiotherapy, to be predicted by medication intake, and by catastrophizing at one year from discharge, the latter in line with our result. As in our study, the outcome was assessed as a minimal clinical important difference, but was based on the Northwick neck pain questionnaire.

Furthermore, we found four reports on non-specific neck pain predictive models with reasonably similar outcomes, methods and follow-up time as in the present study.[33-36] However, all four reports included both male and female patients with different durations of pain, and were not exclusively performed in the course of physiotherapy. Similar to us, Hill et al. and Verhagen et al. found the psychological factors catastrophizing and depression/distress to predict their outcomes.[33 36] Further, baseline neck disability and treatment expectations were included in the models by Hill et al. and by Kjellman et al.[33 35] Other factors in their models were; pain intensity, age, concomitant back pain, manual social class, well-being and somatisation, whereof we have considered age and pain intensity but not found them to be predictors in our study.[33 35 36] Shellingerhout et al. presented a predictive model with a set of nine predictors for global perceived recovery in an adult primary care population.[34] None of the predictors found were similar to our predictors, a discrepancy that may be explained by different study settings and population compared to our study. In their population only 34% reported chronic neck pain and 60% were women. Further, only 28% of the patients were referred to physiotherapy while the others were referred to "usual care", spinal manipulation or a

For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

BMJ Open: first published as 10.1136/bmjopen-2018-024557 on 24 April 2019. Downloaded from http://bmjopen.bmj.com/ on May 15, 2025 at Department GEZ-LTA Erasmushogeschool . Protected by copyright, including for uses related to text and data mining, AI training, and similar technologies.

behaviour graded activity program. Even though Shellingerhout et al. reported a model including nine predictors their model reached almost exactly the same predictive ability as our model, an AUC of 0.66 compared to our 0.67. One could speculate that as prognostic factors in research related to neck pain most often are weak, reaching higher levels of predictive ability may be hard even with large samples and well conducted analyses.[5 9]

Our study meets most of the important criteria for deriving predictive models in relation to musculoskeletal disorders and physiotherapy suggested by Beneciuk et al.; a well-defined study population, longer follow-up times than six months and psychological and psychosocial assessments incorporated in the model-development. Other strengths of our study are a follow-up rate of 82% and a low number of missing data. We used longitudinal analyses (GEE), something we consider an advantage when dealing with recurrent problems.[20] Further, we used clinical important change for the PGICS outcome measure based on the IMMPACT recommendations, and for the NDI outcome measure based on responsiveness analyses in which the same sample as in the present study was included.[25 27] The use of conservative "cut-points" for the Wald test in the selection procedure in order to decrease the risk of type II errors, are also supported in literature.[30-32]

Our sample size of 89 participants could be regarded as small when conducting a prediction study. A small sample size increases the risk of over-dispersion during analyses. However, the sample size was large enough to ensure the recommendations of 10 to 15 participants for each prognostic variable included in the multivariable analyses.[30 31 37] Moreover, as we used GEE analyses, the outcome observations increased when each participant contributed with one to three outcome observations, which resulted in about 250 observations in each of the final models.

Our study also has limitations. It was based on secondary analyses of data, possibly limiting information on additional prognostic factors that may have contributed to the derivation of the models. Of the 108 women included at baseline, 19 did not respond to the three follow-ups and were excluded from the study population. They showed similar characteristics as the included women except for an average pain intensity with a median of 6.5 compared to a median of 5 in the study population. Therefore, attrition might have influenced the results. Some of the participants were

For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

BMJ Open: first published as 10.1136/bmjopen-2018-024557 on 24 April 2019. Downloaded from http://bmjopen.bmj.com/ on May 15, 2025 at Department GEZ-LTA Erasmushogeschool . Protected by copyright, including for uses related to text and data mining, AI training, and similar technologies.

recruited by advertisement and could have different characteristics than ordinary health care patients, why the results may have been influenced by the methods used to recruit the participants. However, our study population had similar baseline levels of average pain intensity, neck pain-related disability and fear of movement as in the study by Shellingerhout et al. investigating prognostic factor for neck pain in a sample of patients referred to primary care.[34] Their population was somewhat younger and included males (39%). Considering the strengths and limitations of our study, we believe our findings to be valid and reproducible.

Predictive models are important as they can be used to inform health care providers and patients, support clinical research and allow for informed decisions to improve outcomes. The clinical implication of our study findings is that baseline neck disability seems to be a highly important factor to consider in this context as a higher baseline disability indicated higher odds for recovery in both our models. This is in line with findings by Bot et al. exploring predictors for patients with neck pain in general practice.[38] Furthermore, psychological factors and recovery expectations are important factors to consider in the clinical course of physiotherapy concerning women with chronic neck pain. As psychological factors and expectations are modifiable they may be targeted in order to increase the possibility for short- and long-term improvement in the management of these women. The information about the prognostic factors and the outcomes included in our models is easily collected at the first consultation by a physiotherapist, and the models could be a valuable tool to help physiotherapists manage these patients.

The predictive ability of our models reach only acceptable levels indicating that there are still factors missing that could predict the outcome. Therefore, it would be valuable to include variables in future investigations that were not included in the present study, such for example tobacco use, alcohol consumption and workplace related factors. A predictive model development, including internal validation, is only the first step in the process of deriving a model that could be implemented in clinic, and should be followed by external validation, and investigations of impact in clinical practice before implementation.[12] Because all women in our sample underwent physiotherapy, our predictive models

For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

BMJ Open: first published as 10.1136/bmjopen-2018-024557 on 24 April 2019. Downloaded from http://bmjopen.bmj.com/ on May 15, 2025 at Department GEZ-LTA Erasmushogeschool . Protected by copyright, including for uses related to text and data mining, AI training, and similar technologies.

should be restricted to this population and setting. We do not know if the models are valid for other populations and other health care providers until externally validated in such context.

CONCLUSION

The developed predictive models evaluating clinical important improvement from chronic non-specific neck pain among women in the clinical course of physiotherapy were robust and showed acceptable predictive ability. Neck pain-related disability, depression, catastrophizing and recovery expectations seems to be factors that can be of guidance for physiotherapists trying to predict the chance of short- and long-term clinical important improvement in these patients. With the exception of neck pain-related disability, different prognostic factors appeared in the models depending on the outcome measure. The results also imply that the outcome predicted by a prognostic factor, exemplified by catastrophizing in one of the models, may be modified over time. The study is the first step in the development of the predictive models. The models have to be externally evaluated in different neck pain populations, and tested in clinical settings before implemented in clinic.

Author contributions: T Bohman, M Björklund and M Bottai contributed to the design of the study. T Bohman made the statistical analyses supported by M Bottai and wrote the first manuscript version. All authors contributed to the interpretation of the data and critically revised all versions of the manuscript and finally approved the last version.

Acknowledgements:

We thank Maria Frykman and Thomas Rudolfsson for excellent administration and data acquisition.

Funding:

The study was funded by Alfta Research Foundation, grants from the Swedish Council for Working Life and Social Research (2006-1162), Länsförsäkringar Forskning och Framtid (51-1010/06) and Forte Centre Working Life “The body at work – from problem to potential” (2009-1761).

Competing interests: None declared.

For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

BMJ Open: first published as 10.1136/bmjopen-2018-024557 on 24 April 2019. Downloaded from http://bmjopen.bmj.com/ on May 15, 2025 at Department GEZ-LTA Erasmushogeschool . Protected by copyright, including for uses related to text and data mining, AI training, and similar technologies.

Ethical approval: The ethics review board in Uppsala, Sweden, approved the study (Registration nr. 207/206).

Data sharing: No additional data available.

Transparency: The corresponding author (T Bohman) affirms that the manuscript is an honest, accurate, and transparent account of the study being reported; that no important aspects of the study have been omitted; and that any discrepancies from the study as planned have been explained.

Figure 1. Included participants and progress of participants along the follow-up period concerning the outcome measures. RCT: Randomised controlled trial. PGICS: The Patient Global Impression of Change Scale. NDI: The Neck Disability Index.

REFERENCES

1. Hogg-Johnson S, van der Velde G, Carroll LJ, et al. The burden and determinants of neck pain in the general population: results of the Bone and Joint Decade 2000-2010 Task Force on Neck Pain and Its Associated Disorders. *Spine (Phila Pa 1976)* 2008;33(4 Suppl):S39-51. doi: 10.1097/BRS.0b013e31816454c8 [published Online First: 2008/02/07]

2. Vos T, Allen C, Arora M, et al. Global, regional, and national incidence, prevalence, and years lived with disability for 310 diseases and injuries, 1990–2015: a systematic analysis for the Global Burden of Disease Study 2015. *The Lancet* 2016;388(10053):1545-602.

3. Hoy D, March L, Woolf A, et al. The global burden of neck pain: estimates from the global burden of disease 2010 study. *Ann Rheum Dis* 2014;73(7):1309-15. doi: 10.1136/annrheumdis-2013-204431

4. The burden of musculoskeletal conditions at the start of the new millennium. World Health Organ Tech Rep Ser 2003;919:i-x, 1-218, back cover. [published Online First: 2003/12/19]

5. Carroll LJ, Hogg-Johnson S, van der Velde G, et al. Course and prognostic factors for neck pain in the general population: results of the Bone and Joint Decade 2000-2010 Task Force on Neck

For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

BMJ Open: first published as 10.1136/bmjopen-2018-024557 on 24 April 2019. Downloaded from http://bmjopen.bmj.com/ on May 15, 2025 at Department GEZ-LTA Erasmushogeschool . Protected by copyright, including for uses related to text and data mining, AI training, and similar technologies.

Pain and Its Associated Disorders. *Spine* 2008;33(4 Suppl):S75-82. doi: 10.1097/BRS.0b013e31816445be [published Online First: 2008/02/07]

6. Vasseljen O, Woodhouse A, Bjørngaard JH, et al. Natural course of acute neck and low back pain in the general population: The HUNT study. *Pain* 2013;154(8):1237-44. doi: 10.1016/j.pain.2013.03.032

7. Hemingway H, Croft P, Perel P, et al. Prognosis research strategy (PROGRESS) 1: a framework for researching clinical outcomes. *BMJ* 2013;346:e5595. [published Online First: 2013/02/07]

8. Guzman J, Haldeman S, Carroll LJ, et al. Clinical practice implications of the Bone and Joint Decade 2000-2010 Task Force on Neck Pain and Its Associated Disorders: from concepts and findings to recommendations. *Spine* 2008;33(4 Suppl):S199-213. doi: 10.1097/BRS.0b013e3181644641 [published Online First: 2008/02/07]

9. Walton DM, Carroll LJ, Kasch H, et al. An Overview of Systematic Reviews on Prognostic Factors in Neck Pain: Results from the International Collaboration on Neck Pain (ICON) Project. *The Open Orthopaedics Journal* 2013;7:494-505. doi: 10.2174/1874325001307010494

10. Hurwitz EL, Carragee EJ, van der Velde G, et al. Treatment of neck pain: noninvasive interventions: results of the Bone and Joint Decade 2000-2010 Task Force on Neck Pain and Its Associated Disorders. *J Manipulative Physiol Ther* 2009;32(2 Suppl):S141-75. doi: S0161-4754(08)00344-8 [published Online First: 2009/03/11]

11. Beattie P, Nelson R. Clinical prediction rules: what are they and what do they tell us? *Aust J Physiother* 2006;52(3):157-63. doi: 10.1016/S0004-9514(06)70024-1 [published Online First: 2006/09/01]

12. Steyerberg EW, Moons KG, van der Windt DA, et al. Prognosis Research Strategy (PROGRESS) 3: prognostic model research. *PLoS Med* 2013;10(2):e1001381. doi: 10.1371/journal.pmed.1001381 [published Online First: 2013/02/09]

13. Bohman T, Alfredsson L, Hallqvist J, et al. The influence of self-reported leisure time physical activity and the body mass index on recovery from persistent back pain among men and

For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

BMJ Open: first published as 10.1136/bmjopen-2018-024557 on 24 April 2019. Downloaded from http://bmjopen.bmj.com/ on May 15, 2025 at Department GEZ-LTA Erasmushogeschool . Protected by copyright, including for uses related to text and data mining, AI training, and similar technologies.

women: a population-based cohort study. *BMC Public Health* 2013;13(1):385. doi: 10.1186/1471-2458-13-385

14. Cote P, Cassidy JD, Carroll LJ, et al. The annual incidence and course of neck pain in the general population: a population-based cohort study. *Pain* 2004;112(3):267-73. doi: 10.1016/j.pain.2004.09.004

15. Messing K, Stock SR, Tissot F. Should studies of risk factors for musculoskeletal disorders be stratified by gender? Lessons from the 1998 Quebec Health and Social Survey (vol 35, pg 96, 2009). *Scand J Work Env Hea* 2009;35(5):400-00. doi: 10.5271/sjweh.1310

16. van Oort L, van den Berg T, Koes BW, et al. Preliminary state of development of prediction models for primary care physical therapy: a systematic review. *J Clin Epidemiol* 2012;65(12):1257-66. doi: 10.1016/j.jclinepi.2012.05.007

17. Cecchi F, Molino-Lova R, Paperini A, et al. Predictors of short- and long-term outcome in patients with chronic non-specific neck pain undergoing an exercise-based rehabilitation program: a prospective cohort study with 1-year follow-up. *Intern Emerg Med* 2011;6(5):413-21. doi: 10.1007/s11739-010-0499-x [published Online First: 2010/12/15]

18. Pool JJ, Ostelo RW, Knol D, et al. Are psychological factors prognostic indicators of outcome in patients with sub-acute neck pain? *Man Ther* 2010;15(1):111-6. doi: 10.1016/j.math.2009.08.001 [published Online First: 2009/09/01]

19. Fitzmaurice GM. Applied longitudinal analysis. Hoboken, N.J.: Hoboken, N.J. : Wiley-Interscience 2004:291-315.

20. Hoogendoorn WE, Bongers PM, de Vet HC, et al. Comparison of two different approaches for the analysis of data from a prospective cohort study: an application to work related risk factors for low back pain. *Occup Environ Med* 2002;59(7):459-65. doi: 10.1136/oem.59.7.459 [published Online First: 2002/07/11]

21. Rudolfsson T, Djupsjobacka M, Hager C, et al. Effects of neck coordination exercise on sensorimotor function in chronic neck pain: a randomized controlled trial. *J Rehabil Med* 2014;46(9):908-14. doi: 10.2340/16501977-1869 [published Online First: 2014/09/04]

For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

BMJ Open: first published as 10.1136/bmjopen-2018-024557 on 24 April 2019. Downloaded from http://bmjopen.bmj.com/ on May 15, 2025 at Department GEZ-LTA Erasmushogeschool . Protected by copyright, including for uses related to text and data mining, AI training, and similar technologies.

22. Margolis RB, Tait RC, Krause SJ. A rating system for use with patient pain drawings. *Pain* 1986;24(1):57-65. doi: 10.1016/0304-3959(86)90026-6 [published Online First: 1986/01/01]

23. Atroshi I, Gummesson C, Andersson B, et al. The disabilities of the arm, shoulder and hand (DASH) outcome questionnaire: reliability and validity of the Swedish version evaluated in 176 patients. *Acta Orthop Scand* 2000;71(6):613-8. doi: 10.1080/000164700317362262

24. Dworkin RH, Turk DC, Farrar JT, et al. Core outcome measures for chronic pain clinical trials: IMMPACT recommendations. *Pain* 2005;113(1-2):9-19. doi: 10.1016/j.pain.2004.09.012 [published Online First: 2004/12/29]

25. Dworkin RH, Turk DC, Wyrwich KW, et al. Interpreting the clinical importance of treatment outcomes in chronic pain clinical trials: IMMPACT recommendations. *J Pain* 2008;9(2):105-21. doi: 10.1016/j.jpain.2007.09.005 [published Online First: 2007/12/07]

26. Vernon H. The Neck Disability Index: state-of-the-art, 1991-2008. *J Manipulative Physiol Ther* 2008;31(7):491-502. doi: 10.1016/j.jmpt.2008.08.006 [published Online First: 2008/09/23]

27. Bjorklund M, Wiitavaara B, Heiden M. Responsiveness and minimal important change for the ProFitMap-neck questionnaire and the Neck Disability Index in women with neck-shoulder pain. *Qual Life Res* 2017;26(1):161-70. doi: 10.1007/s11136-016-1373-8 [published Online First: 2016/08/11]

28. Carroll LJ, Hogg-Johnson S, Cote P, et al. Course and prognostic factors for neck pain in workers: results of the Bone and Joint Decade 2000-2010 Task Force on Neck Pain and Its Associated Disorders. *Spine (Phila Pa 1976)* 2008;33(4 Suppl):S93-100. doi: 10.1097/BRS.0b013e31816445d4 [published Online First: 2008/02/07]

29. Bruls VE, Bastiaenen CH, de Bie RA. Prognostic factors of complaints of arm, neck, and/or shoulder: a systematic review of prospective cohort studies. *Pain* 2015;156(5):765-88. doi: 10.1097/j.pain.0000000000000117 [published Online First: 2015/02/07]

30. Steyerberg EW. Clinical Prediction Models: A practical approach to development, validation, and updating. 1 ed. New York: Springer Science 2009.

For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

BMJ Open: first published as 10.1136/bmjopen-2018-024557 on 24 April 2019. Downloaded from http://bmjopen.bmj.com/ on May 15, 2025 at Department GEZ-LTA Erasmushogeschool . Protected by copyright, including for uses related to text and data mining, AI training, and similar technologies.

31. Vittinghoff E, Glidden DV, Shiboski SC, et al. Regression Methods in Biostatistics, Linear, Logistic, Survival, and Repeated Measures Models. 2nd ed. New York, USA: Springer New York 2012.

32. Hosmer DW, Lemeshow S. Applied logistic regression. 2nd ed. New York ; Chichester: Wiley 2000.

33. Hill JC, Lewis M, Sim J, et al. Predictors of poor outcome in patients with neck pain treated by physical therapy. *Clin J Pain* 2007;23(8):683-90. doi: 10.1097/AJP.0b013e3181468e67 [published Online First: 2007/09/22]

34. Schellingerhout JM, Heymans MW, Verhagen AP, et al. Prognosis of patients with nonspecific neck pain: development and external validation of a prediction rule for persistence of complaints. *Spine (Phila Pa 1976)* 2010;35(17):E827-35. doi: 10.1097/BRS.0b013e3181d85ad5 [published Online First: 2010/07/16]

35. Kjellman G, Skargren E, Oberg B. Prognostic factors for perceived pain and function at one-year follow-up in primary care patients with neck pain. *Disabil Rehabil* 2002;24(7):364-70. doi: 10.1080/10.1080/09638280110101532 [published Online First: 2002/05/23]

36. Verhagen AP, Karels CH, Schellingerhout JM, et al. Pain severity and catastrophising modify treatment success in neck pain patients in primary care. *Man Ther* 2010;15(3):267-72. doi: 10.1016/j.math.2010.01.005 [published Online First: 2010/02/09]

37. Beneciuk JM, Bishop MD, George SZ. Clinical prediction rules for physical therapy interventions: a systematic review. *Phys Ther* 2009;89(2):114-24. doi: 10.2522/ptj.20080239 [published Online First: 2008/12/20]

38. Bot SD, van der Waal JM, Terwee CB, et al. Predictors of outcome in neck and shoulder symptoms: a cohort study in general practice. *Spine* 2005;30(16):E459-E70. doi: 10.1097/01.brs.0000174279.44855.02

39. Turk DC, Melzack R. Handbook of pain assessment. 3rd ed. ed. New York ; London: Guilford 2011.

For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

BMJ Open: first published as 10.1136/bmjopen-2018-024557 on 24 April 2019. Downloaded from http://bmjopen.bmj.com/ on May 15, 2025 at Department GEZ-LTA Erasmushogeschool . Protected by copyright, including for uses related to text and data mining, AI training, and similar technologies.

40. Svanborg P, Asberg M. A new self-rating scale for depression and anxiety states based on the Comprehensive Psychopathological Rating Scale. *Acta Psychiatr Scand* 1994;89(1):21-8. doi: 10.1111/j.1600-0447.1994.tb01480.x [published Online First: 1994/01/01]

41. Cleland JA, Fritz JM, Childs JD. Psychometric properties of the Fear-Avoidance Beliefs Questionnaire and Tampa Scale of Kinesiophobia in patients with neck pain. *Am J Phys Med Rehabil* 2008;87(2):109-17. doi: 10.1097/PHM.0b013e31815b61f1 [published Online First: 2007/11/13]

42. Vlaeyen JW, Kole-Snijders AM, Rotteveel AM, et al. The role of fear of movement/(re)injury in pain disability. *J Occup Rehabil* 1995;5(4):235-52. doi: 10.1007/bf02109988 [published Online First: 1995/12/01]

43. Jensen IB, Linton SJ. Coping strategies questionnaire (CSQ): Reliability of the swedish version of the CSQ. *Cogn Behav Ther* 1993;22(3-4):139-45. doi: 10.1080/16506079309455940

44. Bergstrom G, Jensen IB, Bodin L, et al. Reliability and factor structure of the Multidimensional Pain Inventory--Swedish Language Version (MPI-S). *Pain* 1998;75(1):101-10. doi: 10.1016/S0304-3959(97)00210-8 [published Online First: 1998/04/16]

45. Wolfe F, Smythe HA, Yunus MB, et al. The american college of rheumatology 1990 criteria for the classification of fibromyalgia. *Arthritis & Rheumatism* 1990;33(2):160-72. doi: 10.1002/art.1780330203

46. Ekblom-Bak E, Hellenius ML, Ekblom O, et al. Independent associations of physical activity and cardiovascular fitness with cardiovascular risk in adults. *Eur J Cardiovasc Prev Rehabil* 2010;17(2):175-80. doi: 10.1097/HJR.0b013e32833254f2 [published Online First: 2009/10/08]

47. Leijon O, Wiktorin C, Harenstam A, et al. Validity of a self-administered questionnaire for assessing physical work loads in a general population. *J Occup Environ Med* 2002;44(8):724-35. doi: 10.1097/00043764-200208000-00007 [published Online First: 2002/08/21]

For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

BMJ Open: first published as 10.1136/bmjopen-2018-024557 on 24 April 2019. Downloaded from http://bmjopen.bmj.com/ on May 15, 2025 at Department GEZ-LTA Erasmushogeschool . Protected by copyright, including for uses related to text and data mining, AI training, and similar technologies.

BMJ Open: first published as 10.1136/bmjopen-2018-024557 on 24 April 2019. Downloaded from http://bmjopen.bmj.com/ on May 15, 2025 at Department GEZ-LTA Erasmushogeschool . Protected by copyright, including for uses related to text and data mining, AI training, and similar technologies.

For peer review only

For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

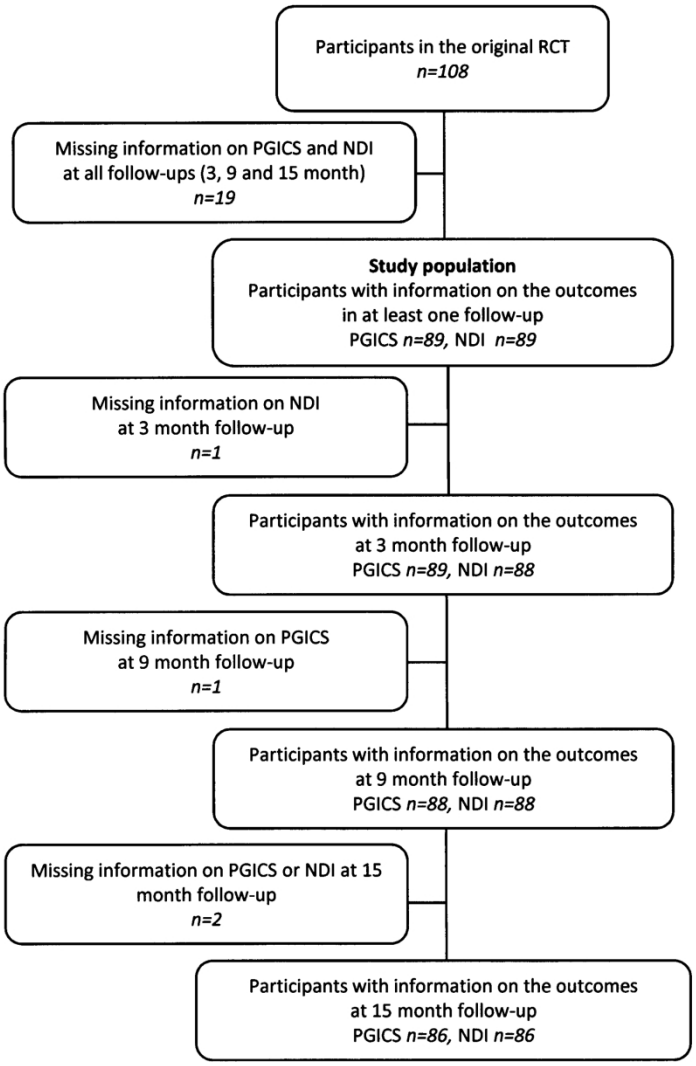

Figure 1. Included participants and progress of participants along the follow-up period concerning the outcome measures. RCT: Randomised controlled trial. PGICS: The Patient Global Impression of Change Scale. NDI: The Neck Disability Index.

206x296mm (300 x 300 DPI)

BMJ Open: first published as 10.1136/bmjopen-2018-024557 on 24 April 2019. Downloaded from http://bmjopen.bmj.com/ on May 15, 2025 at Department GEZ-LTA Erasmushogeschool . Protected by copyright, including for uses related to text and data mining, AI training, and similar technologies.

TRIPOD Checklist: Prediction Model Development

Section/Topic	Item	Checklist Item	Page
Title and abstract			
Title	1	Identify the study as developing and/or validating a multivariable prediction model, the target population, and the outcome to be predicted.	1
Abstract	2	Provide a summary of objectives, study design, setting, participants, sample size, predictors, outcome, statistical analysis, results, and conclusions.	2-3
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.	4-5
	3b	Specify the objectives, including whether the study describes the development or validation of the model or both.	5
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.	5-6
	4b	Specify the key study dates, including start of accrual; end of accrual; and, if applicable, end of follow-up.	6
Participants	5a	Specify key elements of the study setting (e.g., primary care, secondary care, general population) including number and location of centres.	6
	5b	Describe eligibility criteria for participants.	6
	5c	Give details of treatments received, if relevant.	NA
Outcome	6a	Clearly define the outcome that is predicted by the prediction model, including how and when assessed.	6-7
	6b	Report any actions to blind assessment of the outcome to be predicted.	NA
Predictors	7a	Clearly define all predictors used in developing or validating the multivariable prediction model, including how and when they were measured.	7, 8, Tab 1
	7b	Report any actions to blind assessment of predictors for the outcome and other predictors.	NA
Sample size	8	Explain how the study size was arrived at.	Fig 1
Missing data	9	Describe how missing data were handled (e.g., complete-case analysis, single imputation, multiple imputation) with details of any imputation method.	11
Statistical analysis methods	10a	Describe how predictors were handled in the analyses.	12, Tab 1
	10b	Specify type of model, all model-building procedures (including any predictor selection), and method for internal validation.	12-13
	10d	Specify all measures used to assess model performance and, if relevant, to compare multiple models.	12-13
Risk groups	11	Provide details on how risk groups were created, if done.	NA
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.	Fig 1
	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.	Fig 1, Tab 2
Model development	14a	Specify the number of participants and outcome events in each analysis.	10, Tab 3, Tab 4
	14b	If done, report the unadjusted association between each candidate predictor and outcome.	Tab 3
Model specification	15a	Present the full prediction model to allow predictions for individuals (i.e., all regression coefficients, and model intercept or baseline survival at a given time point).	Tab 4
	15b	Explain how to the use the prediction model.	1-19, 22-23
Model performance	16	Report performance measures (with CIs) for the prediction model.	Tab 4
Discussion			
Limitations	18	Discuss any limitations of the study (such as nonrepresentative sample, few events per predictor, missing data).	21-22
Interpretation	19b	Give an overall interpretation of the results, considering objectives, limitations, and results from similar studies, and other relevant evidence.	19-21
Implications	20	Discuss the potential clinical use of the model and implications for future research.	22-23
Other information			
Supplementary information	21	Provide information about the availability of supplementary resources, such as study protocol, Web calculator, and data sets.	24
Funding	22	Give the source of funding and the role of the funders for the present study.	24

We recommend using the TRIPOD Checklist in conjunction with the TRIPOD Explanation and Elaboration document.

BMJ Open: first published as 10.1136/bmjopen-2018-024557 on 24 April 2019. Downloaded from http://bmjopen.bmj.com/ on May 15, 2025 at Department GEZ-LTA Erasmushogeschool . Protected by copyright, including for uses related to text and data mining, AI training, and similar technologies.

BMJ Open

Predictive models for short- and long-term improvement in women under physiotherapy for chronic disabling neck pain: a longitudinal cohort study

Journal:	*BMJ Open*
Manuscript ID	bmjopen-2018-024557.R1
Article Type:	Research
Date Submitted by the Author:	20-Oct-2018
Complete List of Authors:	Bohman, Tony; Karolinska Institutet, Dep. of Neurobiology, Care Sciences and Society; Karolinska Institutet, Institute of Environmental Medicine Bottai, Matteo; Karolinska Institutet, Institue of Environmental Medicine Björklund, Martin; University of Gävle, Department of Occupational and Public Health Sciences; Umeå University, Department of Community Medicine and Rehabilitation
Primary Subject Heading:	Epidemiology
Secondary Subject Heading:	Complementary medicine, Medical management
Keywords:	prediction, prognosis, non-specific neck pain, longitudinal analyses, cohort, clinical important improvement

SCHOLARONE™
Manuscripts

BMJ Open: first published as 10.1136/bmjopen-2018-024557 on 24 April 2019. Downloaded from http://bmjopen.bmj.com/ on May 15, 2025 at Department GEZ-LTA Erasmushogeschool . Protected by copyright, including for uses related to text and data mining, AI training, and similar technologies.

Predictive models for short- and long-term improvement in women under physiotherapy for chronic disabling neck pain: a longitudinal cohort study

Tony Bohman, PhD[1,2], Matteo Bottai, ScD[3], Martin Björklund, PhD[4,5]

[1] Department of Neurobiology, Care Sciences and Society, Division of Physiotherapy, Karolinska Institutet, 23 100, SE-14183, Stockholm, Sweden, [2] Unit of Cardiovascular Epidemiology, Institute of Environmental Medicine, Karolinska Institutet, Box 210, SE-17177, Stockholm, Sweden, [3] Unit of Biostatistics, Institute of Environmental Medicine, Karolinska Institutet, Box 210, SE-17177, Stockholm, Sweden, [4] Department of Occupational and Public Health Sciences, Centre for Musculoskeletal Research, University of Gävle, Gävle, Sweden, [5] Department of Community Medicine and Rehabilitation, Umeå University, Umeå, Sweden

Corresponding author:
Tony Bohman, Department of Neurobiology, Care Sciences and Society, Karolinska Institutet, 23 100, SE-14183, Stockholm, Sweden
e-mail; tony.bohman@ki.se, cellphone; +46 70 299 62 63

Key words; prediction, prognosis, non-specific neck pain, neck pain, longitudinal analyses, cohort, clinical important improvement, discrimination
Word count: 3952
Figures: 1
Tables: 4
References: 48
Supplementary files: 0

For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

BMJ Open: first published as 10.1136/bmjopen-2018-024557 on 24 April 2019. Downloaded from http://bmjopen.bmj.com/ on May 15, 2025 at Department GEZ-LTA Erasmushogeschool . Protected by copyright, including for uses related to text and data mining, AI training, and similar technologies.

1

For peer review only

BMJ Open: first published as 10.1136/bmjopen-2018-024557 on 24 April 2019. Downloaded from http://bmjopen.bmj.com/ on May 15, 2025 at Department GEZ-LTA Erasmushogeschool . Protected by copyright, including for uses related to text and data mining, AI training, and similar technologies.

For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

ABSTRACT

Objectives

To develop predictive models for short- and long-term clinically important improvement in women with non-specific chronic disabling neck pain during the clinical course of physiotherapy.

Design

Longitudinal cohort study based on data from a randomized controlled trial evaluating short- and long-term effects on sensorimotor function over eleven weeks of physiotherapy.

Participants and settings

Eighty-nine women aged 31-65 years with non-specific chronic disabling neck pain from Gävle, Sweden.

Measures

The outcome, clinically important improvement, was measured with the Patient Global Impression of Change Scale (PGICS) and the Neck Disability Index (NDI), assessed by self-administered questionnaires at 3, 9 and 15 months from the start of the interventions (baseline). Twelve baseline prognostic factors were considered in the analyses. The predictive models were built using random-effects logistic regression. The predictive ability of the models was measured by the area under the receiver operating characteristic curve (AUC). Their internal validity was assessed with cross-validation using the bootstrap resampling technique.

Results

The prognostic factors of short- and long-term improvement in the final models were: neck disability and age for the PGICS outcome, and neck disability, depression and catastrophizing for the NDI outcome. In the NDI model, the effect of catastrophizing was modified by time. The cross-validated AUC was 0.64 (95% CI; 0.55-0.73) for PGICS and 0.67 (95% CI; 0.59-0.75) for NDI.

For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

BMJ Open: first published as 10.1136/bmjopen-2018-024557 on 24 April 2019. Downloaded from http://bmjopen.bmj.com/ on May 15, 2025 at Department GEZ-LTA Erasmushogeschool . Protected by copyright, including for uses related to text and data mining, AI training, and similar technologies.

Conclusion

The predictive models of clinical important improvement in the clinical course of physiotherapy of women with chronic non-specific neck pain showed acceptable predictive ability. Age, neck disability and psychological factors seems to be important predictors of improvement, and may inform clinical decisions about physiotherapy in women with chronic neck pain. Before using these models in clinical practice, however, they should be validated in other populations and tested in clinical settings.

Article summary

Strengths and limitations of this study

- Strengths of this study are a well-defined sample and thorough development of predictive models.
- The longitudinal design with a short- and long follow-up time, and the inclusion of biopsychosocial prognostic factors in the analyses further strengthens the study.
- A possible limitation of this study is the relatively small sample.

For peer review only

BMJ Open: first published as 10.1136/bmjopen-2018-024557 on 24 April 2019. Downloaded from http://bmjopen.bmj.com/ on May 15, 2025 at Department GEZ-LTA Erasmushogeschool . Protected by copyright, including for uses related to text and data mining, AI training, and similar technologies.

For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

INTRODUCTION

Neck pain is a common health problem and a cause of substantial disability which has a considerable social and economic impact throughout the world.[1] The prevalence of neck pain has increased during the last decades, and in 2015 neck pain and low back pain were the leading causes of disability.[2] Hoy et al. reported that the 2010 global age-standardised prevalence of neck pain was 4.9%, with the highest overall prevalence observed in North America (6.5%) and western Europe (6.3%).[3] Hogg-Johnson et al. estimated the 12-month prevalence of neck pain to range between 30% and 50% and the 12-month prevalence of activity-limiting pain between 1.7% and 11.5%, with a higher prevalence among women.[1] Neck pain often is unrelated to any other specific pathology.[4] Although single episodes of neck pain generally dissolve over time, they are likely recurrent and may become chronic.[5] In a review from 2008 Carroll et al. concluded that 50% to 85% of persons with neck pain do not experience complete resolution of their pain.[5]

Prognostic research can help understand the course and future outcome in individuals with neck pain.[6] Guzman et al. summarised the work of the 2000-2010 Neck Pain Task Force concluding that younger age, no previous pain, good physiological and psychological health, good coping, good social support, exercise and sports, and no prior sick leave may increase the chance of recovery from neck pain.[7] Walton et al. surveyed prognostic factors for prolonged recovery from neck pain in 13 systematic reviews.[8] They found evidence only for past history of musculoskeletal disorders and older age to prolong recovery in non-whiplash related neck pain. For the remaining factors evaluated there was insufficient evidence for the influence on neck pain, and more research was recommended.

Neck-pain patients commonly seek physical therapy, but predicting treatment outcome and prognosis for these patients is challenging.[9] Predictive models based on multiple prognostic factors could guide healthcare providers, such as physiotherapists, in determining which patients are more likely to improve and to help all patients develop informed expectations.[10 11] It is generally recommended to build predictive models that are applicable to a well-defined patient population and the healthcare system.[10]

For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

BMJ Open: first published as 10.1136/bmjopen-2018-024557 on 24 April 2019. Downloaded from http://bmjopen.bmj.com/ on May 15, 2025 at Department GEZ-LTA Erasmushogeschool . Protected by copyright, including for uses related to text and data mining, AI training, and similar technologies.

Women have a higher risk of chronic neck pain than men, and it has been suggested that women should be assessed separately from men in prognostic research.[12 13] Using the search strategy for predictive models in physiotherapy and musculoskeletal complaints suggested by van Oort et al., we found only one study assessing chronic non-specific neck pain, and none with a model specific for women.[14 15]

The individual perception of pain and disability vary during the course of an episode, and the effect of prognostic factors is therefore expected to change over time following physiotherapy.[15 16] The analysis of longitudinal data is effective in evaluating these potential changes over time, as it can separate the change between individuals from that within any given patient. Longitudinal analyses have been recommended in prospective cohort studies on musculoskeletal problems.[17 18] The aim of this study was to develop predictive models for short- and long-term clinically important improvement in women with chronic disabling neck pain in the clinical course of physiotherapy.

METHODS

Design and study population

This longitudinal cohort study sought to develop predictive models, including multiple prognostic factors jointly, for chronic neck pain in women. Predictive models are one of the four themes of the Prognosis Research Strategy Framework for Prognostic Studies.[6 11] Carroll et al. classify predictive models as "Phase II" studies in a 3-level hierarchy of evidence from longitudinal studies, and suggests them suitable for predicting recovery from neck pain.[5]

We used data from a randomized control trial (RCT) evaluating the short- and long-term effects, following eleven weeks of physiotherapy interventions (coordination exercise, strength training and massage), on sensorimotor function in 108 women with non-specific chronic disabling neck pain.[19] The trial was carried out in Gävle, Sweden, in 2008 and was approved by the ethics review board in Uppsala, Sweden. Participants gave their written consent to participate in the RCT.

For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

BMJ Open: first published as 10.1136/bmjopen-2018-024557 on 24 April 2019. Downloaded from http://bmjopen.bmj.com/ on May 15, 2025 at Department GEZ-LTA Erasmushogeschool . Protected by copyright, including for uses related to text and data mining, AI training, and similar technologies.

The RCT included Swedish-speaking women aged 25 to 65 years with non-specific disabling neck pain lasting for 3 months or more (chronic). The women were recruited via the social insurance agency and with advertisement in local papers and invitations at municipality and county council work sites, primary and occupational healthcare units. Non-specific chronic disabling neck pain was defined as neck pain reported by the patient as the "most painful area" along with disability, measured as > 9 normalised points of the first 19 items in the Disability Arm Shoulder Hand questionnaire (DASH).[20 21] These 19 items refer to disability in activities of daily living regarding neck, shoulders and arms. Excluded were individuals with trauma to the head or neck, a diagnosis of rheumatic, neurological, connective tissue, inflammatory or endocrine disease or psychiatric diagnosis affecting their everyday life, fibromyalgia, cancer, stroke, cardiac infarction, diabetes types I, cervical radiculopathy, vestibular disorders, surgery or fracture to the back, neck, or shoulder in the last 3 years or shoulder luxation in the last year. Finally, strenuous exercise more than 3 times per week during the previous 6 months also led to exclusion.[19]

Patient and Public Involvement

As this study was based on secondary data from a RCT, patients were not directly involved in the design and completion of the study.

Data collection and variables

Before the start of the intervention (baseline), participants filled in a self-administered questionnaire, containing instruments and questions to measure the potential prognostic factors. Outcome information was collected by follow-up questionnaires at three, nine and 15 months from baseline. Participants who did not provide information on the outcome at any of the three follow-ups were excluded, resulting in a study population of 89 participants (Figure 1).

Figure 1

Outcome

The Patient Global Impression of Change Scale (PGICS) provided information for the outcome "global

For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

BMJ Open: first published as 10.1136/bmjopen-2018-024557 on 24 April 2019. Downloaded from http://bmjopen.bmj.com/ on May 15, 2025 at Department GEZ-LTA Erasmushogeschool . Protected by copyright, including for uses related to text and data mining, AI training, and similar technologies.

perceived change of general health" by comparing general health at follow-up with general health at baseline. PGICS is a 7-point ordinal Likert scale (very much improved, much improved, minimally improved, not changed, minimally worse, much worse and very much worse).[22] The scale categories were dichotomized into "improved" (very much improved, much improved) and "not improved" (all the other categories). According to the IMMPACT recommendations for clinical important outcomes in chronic pain, the 7- point scale is recommended when assessing general health. The categories "very much improved" and "much improved" reflects what patients consider to be a clinical important improvement in general health.[23] The Neck Disability Index (NDI) provided information for the second outcome.[24] The NDI has 10 items (pain intensity, personal care, lifting, reading, headaches, concentration, work, driving, sleeping and recreational activities) with 6 possible answers in each item, scored 0 (no limitation) to 5 (major limitations). Total score of the NDI range from 0 to 50. The NDI has high reliability, strong internal consistency and strong validity, when compared with other instruments for evaluating patients with neck pain.[24] In the present study we used the normalized NDI (NDI %, 0-100). The minimal important change (MIC) for the NDI % was set equal to 6.3.[25] Using MIC as a cut-off, a dichotomized NDI outcome was constructed for each follow-up, where a clinical important improvement was defined as a NDI % decrease of more than 6.3 between the baseline and the follow-up, and "no improvement" as an increase, or a decrease less than or equal to 6.3 NDI %. Participants with a NDI % of 0 at follow-up were also defined as having a clinical important improvement regardless of the baseline score.

Potential prognostic factors

The selection of potential prognostic factors was based on systematic reviews and prospective studies on the prognosis of non-specific neck pain, clinical considerations and availability in the data (Table 1). Eight potential prognostic factors had support from literature; age, neck disability, average pain intensity, depression, fear of movement, catastrophizing, social support and leisure physical activity. [5 8 26 27] Chronic widespread pain, recovery expectation, physical work load and dual-working were considered potential prognostic factors based on clinical considerations.

For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

BMJ Open: first published as 10.1136/bmjopen-2018-024557 on 24 April 2019. Downloaded from http://bmjopen.bmj.com/ on May 15, 2025 at Department GEZ-LTA Erasmushogeschool . Protected by copyright, including for uses related to text and data mining, AI training, and similar technologies.

Table 1. Potential prognostic factors and corresponding bibliographical references to definition and psychometric properties of the factors.

Potential prognostic factor	Measurement	Categorisation in the analyses
Age	Age at baseline	Continuous
Neck disability[24]	Normalised Neck Disability Index (NDI%)	Continuous, 1-100 0 = "no disability" and 100 = "complete disability"
Average pain intensity[28]	Average pain intensity during the previous week measured on an 11-point Numeric Rating Scale (NRS)	Continuous, 0-10 0 = "no pain" and 10 = "as bad as it could be"
Depression[29]	Self-rating version of the Montgomery Åsberg Depression Rating Scale (MADRS-S)	Continuous, 0-54 0 = "no depressive symptoms" and 54 = "severe depression"
Fear of movement[30 31]	The Tampa scale of kinesiophobia	Continuous, 17-68 A sum score of 17-68 were higher score indicate higher fear of movement
Catastrophizing[32]	The six item catastrophizing subscale from the Coping Strategies Questionnaire (CSQ).	Continuous, 0-36 Each item of the subscale had a score of 0-6 were a high score indicated a high degree of catastrophizing

For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

For peer review only

Protected by copyright, including for uses related to text and data mining, AI training, and similar technologies.
Erasmushogeschool . Downloaded from http://bmjopen.bmj.com/ on May 15, 2025 at Department GEZ-LTA
10.1136/bmjopen-2018-024557 on 24 April 2019.

Social support[33]	Item number 5 and 14 of the Swedish Multidimensional Pain Inventory (MPI-S)	Continuous, 1-12 Each item with a score of 0-6, where 0 = "no social support" and 12 = "high social support"
Recovery expectation[34]	The answer to the question; "Do you think that any intervention or exercise will lead to recovery?"	Continuous, 1-5 5 point ordinal Likert scale from 1 = "No, definitely not" to 5 = "Yes, completely recovered"
Chronic widespread pain[35]	Derived from a pain drawing	Yes; pain in all 4 quadrants of the body together with spinal pain
Leisure physical activity[36]	"How much have you, in general, moved or exerted yourself physically during leisure time in the past year"	- No/low intensity; very little an occasional walk or similar/ every day physical activity like gardening, cleaning/low intensity physical activity e.g. walking or similar at least once a week - Moderate/high intensity; more strenuous physical activity e.g. jogging, swimming etc. at least once a week/regular high intensity physical activity e.g. running, ball sports etc.
Physical workload[37]	"How physically strenuous has your work or daily activity been the past 12 months?"	- Mostly sedentary

For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

For peer review only

10.1136/bmjopen-2018-024557 on 24 April 2019. Downloaded from http://bmjopen.bmj.com/ on May 15, 2025 at Department GEZ-LTA Erasmushogeschool . Protected by copyright, including for uses related to text and data mining, AI training, and similar technologies.

		- Low/heavy work load; low physical work load but mobile/quite physically strenuous work/physically strenuous work
Dual-working	A combination of three items; 1) Working/not working. 2) What does your household look like? 3) Who is primarily responsible for and performing the housework in your family?	- Yes; 1) working, 2) living together with children and/or another adult person and 3) having the responsibility for the housework - No; any other combination of the three items (see the method section)

For peer review only

For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

10.1136/bmjopen-2018-024557 on 24 April 2019. Downloaded from http://bmjopen.bmj.com/ on May 15, 2025 at Department GEZ-LTA Erasmushogeschool . Protected by copyright, including for uses related to text and data mining, AI training, and similar technologies.

Average pain intensity was not limited to neck pain, but all participants reported neck pain as the "most painful area", as this was a criterion for inclusion in the RCT.[19] Dual-working was a combination of three items: 1) Working/not working, 2) What does your household look like? (living alone, living alone with children, living with another adult, living with another adult and children), 3) Who is primarily performing the housework in your family? (myself, someone else, equally shared). The factor dual-working was then dichotomized according to the answers into; yes (working, living with children and/or another adult, and performing the housework) and no (any other combination of the three items). Dual-working has to our knowledge not been evaluated in previous studies, but in our opinion it is possibly associated with the prognosis of neck pain in women.

Statistical methods

Descriptive statistics are presented as means and standard deviations (SD) or median and interquartile range (IQR) when appropriate. The level of the confidence intervals (CI) was set at 95% and that of the tests at 5%. All p-values were two-sided. Stata version 14.2 (StataCorp College Station, TX, USA) was used in the analyses.

Random-effects logistic regression models were used to estimate the probability of a clinically important improvement of the outcomes from baseline to three and 15-months follow-up visits.[17] Data from all three follow-ups were used in the analyses. Random-effects logistic regression can model longitudinal data efficiently, while taking into account the potential dependence of the repeated measures taken on each participant.[17] The regression models were estimated for each of the two outcomes, PGICS and NDI, separately. Both outcomes showed strong associations between the follow-ups. Associations are reported as odds ratios (OR) with 95% CI. The linearity of the relationship between the logit of the probability of the outcome variables and numeric independent variables was verified by means of restricted cubic splines.[17 38] None of the numeric independent variables showed evidence against linearity.

Univariate analyses

For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

BMJ Open: first published as 10.1136/bmjopen-2018-024557 on 24 April 2019. Downloaded from http://bmjopen.bmj.com/ on May 15, 2025 at Department GEZ-LTA Erasmushogeschool . Protected by copyright, including for uses related to text and data mining, AI training, and similar technologies.

Random-effects logistic regressions were used for all potential prognostic factors one at a time to estimate the time-specific OR for each of the two outcome measures, separately. If the interaction term (factor-by-time) was not statistically significant, the analyses were repeated without the interaction term. This resulted in a single OR for the factor from three to 15 months. When the interaction was significant, the OR at three and 15 months were reported separately. Potential prognostic factors with a p-value ≤ 0.2 for the estimated OR were considered candidate factors for the multivariable analyses.[38] Based on an a priori decision of clinical relevance, statistical effect measure modifications were tested between pain intensity and depression or recovery expectations. If the interaction term was statistically significant, this was included in the subsequent analyses.[39]

Developing the models

A sequential backward manual selection procedure with the random-effects logistic regressions was used to build the predictive models.[38] All candidate factors were included in the initial multivariable model. The factor with the highest p-value (Wald-test) were excluded one by one until all factors in the model had a p-value ≤ 0.1.[38] If a candidate factor showed effect-modification with time, then the factor was included together with the effect measure modification in the multivariable model. If the analysis showed signs of collinearity the factor judged most clinically relevant was kept in the model. During the development process, all the multivariable analyses were adjusted for the assigned RCT interventions. "Intervention" was then removed from the final predictive models before evaluating the models and presenting the results. The association between the prognostic factor and the outcome was reported as beta-coefficient (β) with standard error (SE), OR with 95% CI and associated p-value.

Evaluation of the models

The bias corrected area under the receiver operating characteristic curve (AUC) with 95% CI was obtained by cross-validation based on 100 design-matrix bootstrap replicates and used to determine the internally-validated predictive ability of the models.[39] The AUC represents a summary of the sensitivity

For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

BMJ Open: first published as 10.1136/bmjopen-2018-024557 on 24 April 2019. Downloaded from http://bmjopen.bmj.com/ on May 15, 2025 at Department GEZ-LTA Erasmushogeschool . Protected by copyright, including for uses related to text and data mining, AI training, and similar technologies.

and specificity of the model in distinguishing participants who improve during the follow-up period from those who do not. The AUC ranges from 0.5 (no predictive ability) to 1.0 (perfect predictive ability). Overfitting was assessed by calculating the heuristic shrinkage factor.[40] A shrinkage factor of 1.0 indicates no overfitting of the model.

Sensitivity analyses

To compare the study population with that of the non-responders, we used the chi-squared test for categorical variables, and the t-test or the Wilcoxon's rank-sum test for continuous variables.

RESULTS

Study population

Baseline characteristics of the study population are listed in Table 2. The women's age ranged between 31 and 65 years, and all women reported neck pain duration of more than eight months, with a median of 120 months (IQR 60-216). Eighty women (91%) were working and 66 (74%) reported no sick leave because of neck pain during the previous 6 months. Using PGICS as outcome measure 47 (53%) women were categorised as improved at 3-month and 26 (30%) at 15-month follow-up while using NDI as outcome measure 39 (44%) women had improved at 3 months and 31 (36%) at 15 months.

Table 2. Baseline characteristics of the study population, n=89.

Characteristics		Missing (n)[a]
Age median (IQR)	52 (47-59)	0
Neck disability median (IQR)	28 (20-33)	0
Average pain intensity mean (SD)	5.2 (1.6)	0
Depression median (IQR)	8 (6-12)	1
Fear of movement median (IQR)	29 (26-33)	0

For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

BMJ Open: first published as 10.1136/bmjopen-2018-024557 on 24 April 2019. Downloaded from http://bmjopen.bmj.com/ on May 15, 2025 at Department GEZ-LTA Erasmushogeschool . Protected by copyright, including for uses related to text and data mining, AI training, and similar technologies.

Catastrophizing median (IQR)	6 (3-11)	0
Social support mean (SD)	6.2 (3.4)	1
Recovery expectation median (IQR)	4 (3-4)	4
Chronic widespread pain freq (%)		0
Yes	40 (45)	
Leisure physical activity freq (%)		0
No/low intensity	60 (67)	
Moderate/high intensity	29 (33)	
Physical workload freq (%)		1
Mostly sedentary	36 (41)	
Low/heavy work load	52 (59)	
Dual-working freq (%)		4
Yes	38 (45)	

[a] missing answer, IQR; interquartile range, SD; standard deviation, freq; frequency.

Development and evaluation of the predictive model

The univariate analyses are presented in table 3. The follow-up data observations used for the analyses differed slightly between the two outcome measures because of missing responses (Figure 1). No effect measure modification was observed between pain intensity and depression or recovery expectations. In the univariate analyses with PGICS as outcome measure age, neck disability, and average pain intensity met the inclusion criteria for the multivariable analysis. No potential prognostic factor appeared to modify the effect of time. In the corresponding analyses with NDI as outcome measure, five potential prognostic factors met the criteria for the multivariable analysis: age, neck disability, depression, catastrophizing, and leisure physical activity. The effect of catastrophizing changed over time, and an effect measure modification term (catastrophizing x time) was added to the multivariable analysis.

For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

BMJ Open: first published as 10.1136/bmjopen-2018-024557 on 24 April 2019. Downloaded from http://bmjopen.bmj.com/ on May 15, 2025 at Department GEZ-LTA Erasmushogeschool . Protected by copyright, including for uses related to text and data mining, AI training, and similar technologies.

Table 3. Univariate random-effects regression analyses for short and long-term potential prognostic factors with PGICS and NDI as outcome, n=89.

Potential prognostic factor	PGICS				
	n/obs[a]	OR 3–15 m[b]	95% CI	p-value	p-eff.m.[c]
Age*	*89/263*	0.92	0.84, 1.01	0.08	0.75
Neck disability*	*89/263*	1.08	1.01, 1.16	0.03	0.26
Average pain intensity*	*89/263*	1.60	1.00, 2.55	0.05	1.00
Depression	*88/260*	1.04	0.92, 1.19	0.50	0.07
Fear of movement	*89/263*	0.98	0.87, 1.09	0.67	0.48
Catastrophizing	*89/263*	1.06	0.94, 1.20	0.34	0.20
Social support	*88/260*	1.08	0.88, 1.33	0.47	0.57
Recovery expectations	*85/253*	1.74	0.71, 4.25	0.22	0.47
Chronic widespread pain	*89/263*				0.45
No		1.0			
Yes		1.99	0.46, 8.66	0.36	
Leisure physical activity	*89/263*				0.36
No/low intensity		1.0			
Moderate/high intensity		0.77	0.16, 3.65	0.75	
Physical workload	*88/260*				0.64
Mostly sedentary		1.0			
Low to heavy workload		1.35	0.31, 5.86	0.69	
Dual-working	*85/251*				0.41
No		1.0			
Yes		0.77	0.17, 3.39	0.73	
Potential prognostic factor	**NDI**				

For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

BMJ Open: first published as 10.1136/bmjopen-2018-024557 on 24 April 2019. Downloaded from http://bmjopen.bmj.com/ on May 15, 2025 at Department GEZ-LTA Erasmushogeschool . Protected by copyright, including for uses related to text and data mining, AI training, and similar technologies.

	n/obs[a]	OR 3–15 m[b]	95% CI	p-value	p-eff.m.[c]
Age*	89/262	0.96	0.90, 1.02	0.20	0.68
Neck disability*	89/262	1.05	1.01, 1.11	0.02	0.31
Average pain intensity	89/262	1.17	0.84, 1.63	0.35	0.67
Depression*	88/259	0.94	0.86, 1.03	0.17	0.75
Fear of movement	89/262	0.99	0.92, 1.07	0.87	0.88
Catastrophizing*	89/262				0.03
3 m[d]		1.10	0.98, 1.24	0.12	
15 m[e]		0.93	0.83, 1.05	0.23	
Social support	88/259	1.08	0.93, 1.26	0.32	0.72
Recovery expectations	85/253	0.73	0.39, 1.37	0.33	0.37
Chronic widespread pain	89/262				0.10
No		1.0			
Yes		0.72	0.26, 1.99	0.53	
Leisure physical activity*	89/262				0.36
No/low intensity		1.0			
Moderate/high intensity		0.48	0.16, 1.43	0.19	
Physical workload	88/259				0.06
Mostly sedentary		1.0			
Low to heavy workload		1.16	0.41, 3.25	0.78	
Dual-working	85/250				0.16
No		1.0			
Yes		0.55	0.19, 1.58	0.27	

OR=odds ratio, an OR>1 reflects a higher odds of clinical important improvement and an OR<1 reflects a lower odds of clinical important improvement, * Potential prognostic factors included in the development of the multivariable predictive models,

For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

BMJ Open: first published as 10.1136/bmjopen-2018-024557 on 24 April 2019. Downloaded from http://bmjopen.bmj.com/ on May 15, 2025 at Department GEZ-LTA Erasmushogeschool . Protected by copyright, including for uses related to text and data mining, AI training, and similar technologies.

PGICS: Patient Global Impression of Change Scale, NDI: normalized Neck Disability Index, [a] number of participants in the analyses/number of outcome observations in the analyses, [b] odds ratios for clinically important improvement between 3 to 15 months, CI: Confidence interval, [c] p-value for the effect modification over time between 3 to 15 months from baseline, [d and e] results (OR, 95% CI and p-values) for clinically important improvement at 3 and 15 months respectively.

The resulting predictive models from the sequential selection procedure are presented in Table 4. There were no signs of collinearity in the multivariable analyses. Internal validation showed acceptable predictive ability for the models of 0.64 and 0.67 respectively (Table 4). The calculated shrinkage factor was 0.73 for the PGICS model and 0.65 for the NDI model.

Table 4. The final predictive models as a result from the multivariable analyses of clinically important improvement in chronic disabling neck pain with PGICS and NDI as outcomes.

Prognostic factor	**PGICS**, *(89/263)[a]*				
	β	**SE**	**OR**	**95% CI**	**p-value**
Neck disability	0.08	0.04	1.08	1.01, 1.16	0.03
Age	-0.08	0.05	0.92	0.84, 1.01	0.08
AUC (95% CI)[c]	0.64 (0.55, 0.73)				
Prognostic factor	**NDI**, *(88/259)[a]*				
	β	**SE**	**OR**	**95% CI**	**p-value**
Neck disability	0.08	0.03	1.08	1.02, 1.14	0.01
Depression	-0.11	0.05	0.89	0.81, 0.98	0.02
Catastrophizing					
3 months	0.07	0.06	1.08	0.96, 1.21	0.21
15 months	-0.09	0.06	0.92	0.82, 1.03	0.14
x time[b]	-0.01	0.01	0.99	0.97, 1.00	0.03
AUC (95% CI)[c]	0.67 (0.59, 0.75)				

For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

BMJ Open: first published as 10.1136/bmjopen-2018-024557 on 24 April 2019. Downloaded from http://bmjopen.bmj.com/ on May 15, 2025 at Department GEZ-LTA Erasmushogeschool . Protected by copyright, including for uses related to text and data mining, AI training, and similar technologies.

OR=odds ratio, an OR>1 reflects a higher odds of clinical important improvement and an OR<1 reflects a lower odds of clinical important improvement, PGICS: Patient Global Impression of Change Scale, NDI: normalized Neck Disability Index, β: beta coefficient, SE: standard error, CI: confidence interval, [a] number of participants in the analysis/number of outcome observations in the analysis, [b] effect measure modification term in the model; catastrophizing x time, [c] internally validated receiver operating characteristics curve (AUC) with 95% CI.

Sensitivity analyses

Non-responders (n = 19) showed no statistically significant differences in the characteristics from the study population except for average pain intensity, where non-responders had a higher median of 6.5 compared with a median of 5 (p = 0.03) in the study population.

DISCUSSION

We developed and internally validated predictive models for clinically important short- and long-term improvement from chronic disabling neck pain among women in the clinical course of physiotherapy. The models were developed for the "global perceived change of general health" (PGICS) and the Neck Disability Index (NDI), separately. Both models had acceptable predictive ability.[39] The results showed that, when assessing potential biopsychosocial prognostic factors, perceived disabilities related to neck pain, depression, catastrophizing and age are of importance for predicting short- and long-term improvements in these women. Further, we found that prognostic factors could predict different results depending on the follow up time, as for catastrophizing in the NDI model. This is important in the management of patients in clinical settings. Similarly to previous studies, we found that the prognostic factors in the models could differ depending on the outcome.[16 34]

Our results indicate that the odds for clinically important improvement, with PGICS as outcome measure, decrease with age and increase with higher baseline levels of disability related to neck pain. With NDI as an outcome measure, the odds for improvement increased with higher baseline levels of neck pain-related disability and decrease with higher levels of depression. These results were valid over the total follow up

For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

BMJ Open: first published as 10.1136/bmjopen-2018-024557 on 24 April 2019. Downloaded from http://bmjopen.bmj.com/ on May 15, 2025 at Department GEZ-LTA Erasmushogeschool . Protected by copyright, including for uses related to text and data mining, AI training, and similar technologies.

time of 15 months. However, the model indicated increased odds for short-term improvement, but decreased odds for long-term improvement with higher levels of catastrophizing at baseline. This interesting finding was made possible by the longitudinal nature of our study design. To the best of our knowledge, this is the first study using longitudinal analyses in predictive models for neck pain. Interestingly, depression was found to be a predictor even though women with a psychiatric diagnosis affecting their everyday life were excluded from the study.

The relative strength of the incorporated factors in the model should be interpreted with great caution as their independent effect on the outcome were not thoroughly examined.

Our findings are somewhat different from those of other similar studies, because of the different study populations, potential prognostic factors examined, outcomes and follow up times. We found only one prediction study on patients with chronic non-specific neck pain in physiotherapy, but with a study population also including males.[15] Poor outcome was predicted by pain medication at discharge and at one-year follow-up, and by catastrophizing at one-year follow-up, the latter in line with our results. Similarly to our study, the outcome was assessed as a minimal clinical important difference, but was based on the Northwick neck pain questionnaire.

We found four reports on non-specific neck pain predictive models with reasonably similar outcomes, methods and follow-up time as in the present study.[34 41-43] However, all four reports included both male and female patients with different durations of pain (acute, subacute and chronic), and were not performed in the course of physiotherapy only. Similarly to us, Hill et al. and Verhagen et al. found the psychological factors catastrophizing and depression/distress to predict their outcomes.[34 43] Also, baseline neck disability was included in the models by Hill et al. and by Kjellman et al.[34 42] Other factors in their models were; pain intensity, treatment expectations, concomitant back pain, manual social class, well-being and somatisation, while we found that treatment expectations and pain intensity were not important predictors in our study.[34 42 43] Shellingerhout et al. presented a predictive model with a set of nine predictors for global perceived recovery in an adult primary care population.[41] With the exception of age,

For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

BMJ Open: first published as 10.1136/bmjopen-2018-024557 on 24 April 2019. Downloaded from http://bmjopen.bmj.com/ on May 15, 2025 at Department GEZ-LTA Erasmushogeschool . Protected by copyright, including for uses related to text and data mining, AI training, and similar technologies.

none of the predictors found were similar to our predictors, a discrepancy that may be explained by different study settings, population and outcome compared with our study. In their population only 34% reported chronic neck pain and 60% were women. Further, only 28% of the patients were referred to physiotherapy while the others were referred to "usual care", spinal manipulation or a behaviour graded activity program. Even though Shellingerhout et al. reported a model including nine predictors, their predictive ability (AUC = 0.66) was similar to that of our models (AUC of 0.64 and 0.67). One could speculate that as prognostic factors in research related to neck pain most often are weak, reaching higher levels of predictive ability may be hard even with large samples and well conducted analyses.[5 8]

Our study meets most of the important criteria for deriving predictive models in relation to musculoskeletal disorders and physiotherapy suggested by Beneciuk et al.: a well-defined study population, longer follow-up times than six months and psychological and psychosocial assessments incorporated in the model-development.[44] Other strengths of our study are a follow-up rate of 82% and a small number of missing data. We used longitudinal analyses, an advantage when assessing individual change over time.[18] The outcome, clinical important improvement, was based on the IMMPACT recommendations (PGICS), and on responsiveness analyses in which the same sample as in the present study was included (NDI).[23 25] The use of conservative "cut-points" for the Wald test in the selection procedure in order to decrease the risk of type II errors, are also supported in literature.[38 39]

Our sample size of 89 participants could be considered small when conducting a prediction study. A small sample size increases the risk of over-dispersion during analyses. However, the sample size was large enough to ensure the recommendations of 10 to 15 participants for each prognostic variable included in the multivariable analyses.[38 44] Moreover, as we used longitudinal analyses, each participant contributed with one to three outcome observations which resulted in about 260 observations in each of the final models.

Our study also has limitations. It was based on secondary analyses of data, possibly limiting information on additional prognostic factors which could have influenced the derivation of the models. Of the 108

For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

BMJ Open: first published as 10.1136/bmjopen-2018-024557 on 24 April 2019. Downloaded from http://bmjopen.bmj.com/ on May 15, 2025 at Department GEZ-LTA Erasmushogeschool . Protected by copyright, including for uses related to text and data mining, AI training, and similar technologies.

women included at baseline, 19 did not respond to any of the three follow-ups and were excluded from the analyses. They showed similar characteristics as the included women except for an average pain intensity with a median of 6.5 compared with a median of 5 in the study population. Therefore, attrition might have influenced the results. Some of the participants were recruited by advertisement and could have different characteristics than ordinary healthcare patients.[45] However, the baseline levels of average pain intensity, neck pain-related disability and fear of movement in the study were similar to those in the study by Shellingerhout et al., who investigated prognostic factor for neck pain in a sample of patients referred to primary care.[41]

The clinical implication of our study findings is that baseline neck disability seems to be an important factor to consider, as a higher baseline disability was associated with higher odds for clinical important improvement in both our models. This is in line with the findings of Bot et al. in exploring predictors for patients with neck or shoulder pain in general practice.[46] They found, that being more disabled at baseline predicted a larger reduction in disability at 3 and 12 months follow-up. Furthermore, psychological factors are important to consider in the clinical course of physiotherapy concerning women with chronic neck pain. As psychological factors are modifiable they may be targeted in order to increase the possibility for short- and long-term improvement in the management of these women. The information about the prognostic factors and the outcomes included in our models is easily collected at the first consultation by a physiotherapist, and the models could be a valuable tool to help physiotherapists manage these patients.

While the predictive ability of our models was acceptable, it also indicated that there may still be other factors that could help predict the outcome more precisely. It would therefore be valuable to include variables in future investigations that were not included in the present study, like for example lifestyle factors such as tobacco and alcohol use, and psychological factors related to work.[47 48] Our models will make clinicians aware of what factors are important to consider when predicting which patients will have the best chance of a clinical important improvement. Furthermore, our results facilitate future prognostic

For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

BMJ Open: first published as 10.1136/bmjopen-2018-024557 on 24 April 2019. Downloaded from http://bmjopen.bmj.com/ on May 15, 2025 at Department GEZ-LTA Erasmushogeschool . Protected by copyright, including for uses related to text and data mining, AI training, and similar technologies.

research related to chronicity in neck pain. A predictive model development, including internal validation, is only the first step in the process of deriving a model that could be implemented in clinic. A second step should be external validation, for example, by using data from RCTs including other types of interventions targeting chronic neck pain. Finally, further external validation should be done by investigating the impact of the model in clinical practice before implementation.[11] Because all women in our sample underwent physiotherapy, our predictive models should be restricted to this population and setting. The validity in other populations and other healthcare providers will remain unknown until external validations will be available.

CONCLUSION

The developed predictive models evaluating clinical important improvement from chronic non-specific neck pain among women in the clinical course of physiotherapy showed acceptable predictive ability. Age, neck pain-related disability, depression, and catastrophizing seems to be factors that can be of guidance for physiotherapists trying to predict the chance of short- and long-term clinical important improvement in these patients. With the exception of neck pain-related disability, different outcome measures had different sets of prognostic factors. The effect of some factors may be modified by time. The present study is the first step towards developing predictive models for clinical practice. The next steps will include external validations in different neck pain populations and clinical settings.

Author contributions: T Bohman, M Björklund and M Bottai contributed to the design of the study. T Bohman made the statistical analyses supported by M Bottai and wrote the first manuscript version. All authors contributed to the interpretation of the data and critically revised all versions of the manuscript and finally approved the last version.

Acknowledgements:

We thank Maria Frykman and Thomas Rudolfsson for excellent administration and data acquisition.

For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

BMJ Open: first published as 10.1136/bmjopen-2018-024557 on 24 April 2019. Downloaded from http://bmjopen.bmj.com/ on May 15, 2025 at Department GEZ-LTA Erasmushogeschool . Protected by copyright, including for uses related to text and data mining, AI training, and similar technologies.

Funding:

The study was funded by Alfta Research Foundation, grants from the Swedish Council for Working Life and Social Research (2006-1162), Länsförsäkringar Forskning och Framtid (51-1010/06) and Forte Centre Working Life "The body at work – from problem to potential" (2009-1761).

Competing interests: None declared.

Ethical approval: The ethics review board in Uppsala, Sweden, approved the study (Registration nr. 207/206).

Data sharing: No additional data available.

Transparency: The corresponding author (T Bohman) affirms that the manuscript is an honest, accurate, and transparent account of the study being reported; that no important aspects of the study have been omitted; and that any discrepancies from the study as planned have been explained.

Figure 1. Included participants and progress of participants along the follow-up period concerning the outcome measures. RCT: Randomised controlled trial. PGICS: The Patient Global Impression of Change Scale. NDI: The Neck Disability Index.

REFERENCES

1. Hogg-Johnson S, van der Velde G, Carroll LJ, et al. The burden and determinants of neck pain in the general population: results of the Bone and Joint Decade 2000-2010 Task Force on Neck Pain and Its Associated Disorders. *Spine (Phila Pa 1976)* 2008;33(4 Suppl):S39-51.
2. Vos T, Allen C, Arora M, et al. Global, regional, and national incidence, prevalence, and years lived with disability for 310 diseases and injuries, 1990–2015: a systematic analysis for the Global Burden of Disease Study 2015. *The Lancet* 2016;388(10053):1545-602.
3. Hoy D, March L, Woolf A, et al. The global burden of neck pain: estimates from the global burden of disease 2010 study. *Ann Rheum Dis* 2014;73(7):1309-15.

For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

BMJ Open: first published as 10.1136/bmjopen-2018-024557 on 24 April 2019. Downloaded from http://bmjopen.bmj.com/ on May 15, 2025 at Department GEZ-LTA Erasmushogeschool . Protected by copyright, including for uses related to text and data mining, AI training, and similar technologies.

4. The burden of musculoskeletal conditions at the start of the new millennium. World Health Organ Tech Rep Ser 2003;919:i-x, 1-218, back cover.

5. Carroll LJ, Hogg-Johnson S, van der Velde G, et al. Course and prognostic factors for neck pain in the general population: results of the Bone and Joint Decade 2000-2010 Task Force on Neck Pain and Its Associated Disorders. *Spine* 2008;33(4 Suppl):S75-82.

6. Hemingway H, Croft P, Perel P, et al. Prognosis research strategy (PROGRESS) 1: a framework for researching clinical outcomes. *BMJ* 2013;346:e5595.

7. Guzman J, Haldeman S, Carroll LJ, et al. Clinical practice implications of the Bone and Joint Decade 2000-2010 Task Force on Neck Pain and Its Associated Disorders: from concepts and findings to recommendations. *Spine* 2008;33(4 Suppl):S199-213.

8. Walton DM, Carroll LJ, Kasch H, et al. An Overview of Systematic Reviews on Prognostic Factors in Neck Pain: Results from the International Collaboration on Neck Pain (ICON) Project. *The Open Orthopaedics Journal* 2013;7:494-505.

9. Hurwitz EL, Carragee EJ, van der Velde G, et al. Treatment of neck pain: noninvasive interventions: results of the Bone and Joint Decade 2000-2010 Task Force on Neck Pain and Its Associated Disorders. *J Manipulative Physiol Ther* 2009;32(2 Suppl):S141-75.

10. Beattie P, Nelson R. Clinical prediction rules: what are they and what do they tell us? *Aust J Physiother* 2006;52(3):157-63.

11. Steyerberg EW, Moons KG, van der Windt DA, et al. Prognosis Research Strategy (PROGRESS) 3: prognostic model research. *PLoS Med* 2013;10(2):e1001381.

12. Bohman T, Alfredsson L, Hallqvist J, et al. The influence of self-reported leisure time physical activity and the body mass index on recovery from persistent back pain among men and women: a population-based cohort study. *BMC Public Health* 2013;13(1):385.

For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

BMJ Open: first published as 10.1136/bmjopen-2018-024557 on 24 April 2019. Downloaded from http://bmjopen.bmj.com/ on May 15, 2025 at Department GEZ-LTA Erasmushogeschool . Protected by copyright, including for uses related to text and data mining, AI training, and similar technologies.

13. Messing K, Stock SR, Tissot F. Should studies of risk factors for musculoskeletal disorders be stratified by gender? Lessons from the 1998 Quebec Health and Social Survey (vol 35, pg 96, 2009). *Scand J Work Env Hea* 2009;35(5):400-00.

14. van Oort L, van den Berg T, Koes BW, et al. Preliminary state of development of prediction models for primary care physical therapy: a systematic review. *J Clin Epidemiol* 2012;65(12):1257-66.

15. Cecchi F, Molino-Lova R, Paperini A, et al. Predictors of short- and long-term outcome in patients with chronic non-specific neck pain undergoing an exercise-based rehabilitation program: a prospective cohort study with 1-year follow-up. *Intern Emerg Med* 2011;6(5):413-21.

16. Pool JJ, Ostelo RW, Knol D, et al. Are psychological factors prognostic indicators of outcome in patients with sub-acute neck pain? *Man Ther* 2010;15(1):111-6.

17. Fitzmaurice GM. Applied longitudinal analysis. Hoboken, N.J.: Hoboken, N.J. : Wiley-Interscience 2004:325-371.

18. Hoogendoorn WE, Bongers PM, de Vet HC, et al. Comparison of two different approaches for the analysis of data from a prospective cohort study: an application to work related risk factors for low back pain. *Occup Environ Med* 2002;59(7):459-65.

19. Rudolfsson T, Djupsjobacka M, Hager C, et al. Effects of neck coordination exercise on sensorimotor function in chronic neck pain: a randomized controlled trial. *J Rehabil Med* 2014;46(9):908-14.

20. Margolis RB, Tait RC, Krause SJ. A rating system for use with patient pain drawings. *Pain* 1986;24(1):57-65.

21. Atroshi I, Gummesson C, Andersson B, et al. The disabilities of the arm, shoulder and hand (DASH) outcome questionnaire: reliability and validity of the Swedish version evaluated in 176 patients. *Acta Orthop Scand* 2000;71(6):613-8.

22. Dworkin RH, Turk DC, Farrar JT, et al. Core outcome measures for chronic pain clinical trials: IMMPACT recommendations. *Pain* 2005;113(1-2):9-19.

23. Dworkin RH, Turk DC, Wyrwich KW, et al. Interpreting the clinical importance of treatment outcomes in chronic pain clinical trials: IMMPACT recommendations. *J Pain* 2008;9(2):105-21.

For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

BMJ Open: first published as 10.1136/bmjopen-2018-024557 on 24 April 2019. Downloaded from http://bmjopen.bmj.com/ on May 15, 2025 at Department GEZ-LTA Erasmushogeschool . Protected by copyright, including for uses related to text and data mining, AI training, and similar technologies.

24. Vernon H. The Neck Disability Index: state-of-the-art, 1991-2008. *J Manipulative Physiol Ther* 2008;31(7):491-502.

25. Bjorklund M, Wiitavaara B, Heiden M. Responsiveness and minimal important change for the ProFitMap-neck questionnaire and the Neck Disability Index in women with neck-shoulder pain. *Qual Life Res* 2017;26(1):161-70.

26. Carroll LJ, Hogg-Johnson S, Cote P, et al. Course and prognostic factors for neck pain in workers: results of the Bone and Joint Decade 2000-2010 Task Force on Neck Pain and Its Associated Disorders. *Spine (Phila Pa 1976)* 2008;33(4 Suppl):S93-100.

27. Bruls VE, Bastiaenen CH, de Bie RA. Prognostic factors of complaints of arm, neck, and/or shoulder: a systematic review of prospective cohort studies. *Pain* 2015;156(5):765-88.

28. Turk DC, Melzack R. Handbook of pain assessment. 3rd ed. ed. New York ; London: Guilford 2011.

29. Svanborg P, Asberg M. A new self-rating scale for depression and anxiety states based on the Comprehensive Psychopathological Rating Scale. *Acta Psychiatr Scand* 1994;89(1):21-8.

30. Cleland JA, Fritz JM, Childs JD. Psychometric properties of the Fear-Avoidance Beliefs Questionnaire and Tampa Scale of Kinesiophobia in patients with neck pain. *Am J Phys Med Rehabil* 2008;87(2):109-17.

31. Vlaeyen JW, Kole-Snijders AM, Rotteveel AM, et al. The role of fear of movement/(re)injury in pain disability. *J Occup Rehabil* 1995;5(4):235-52.

32. Jensen IB, Linton SJ. Coping strategies questionnaire (CSQ): Reliability of the swedish version of the CSQ. *Cogn Behav Ther* 1993;22(3-4):139-45.

33. Bergstrom G, Jensen IB, Bodin L, et al. Reliability and factor structure of the Multidimensional Pain Inventory--Swedish Language Version (MPI-S). *Pain* 1998;75(1):101-10.

34. Hill JC, Lewis M, Sim J, et al. Predictors of poor outcome in patients with neck pain treated by physical therapy. *Clin J Pain* 2007;23(8):683-90.

35. Wolfe F, Smythe HA, Yunus MB, et al. The american college of rheumatology 1990 criteria for the classification of fibromyalgia. *Arthritis & Rheumatism* 1990;33(2):160-72.

For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

BMJ Open: first published as 10.1136/bmjopen-2018-024557 on 24 April 2019. Downloaded from http://bmjopen.bmj.com/ on May 15, 2025 at Department GEZ-LTA Erasmushogeschool . Protected by copyright, including for uses related to text and data mining, AI training, and similar technologies.

36. Ekblom-Bak E, Hellenius ML, Ekblom O, et al. Independent associations of physical activity and cardiovascular fitness with cardiovascular risk in adults. *Eur J Cardiovasc Prev Rehabil* 2010;17(2):175-80.

37. Leijon O, Wiktorin C, Harenstam A, et al. Validity of a self-administered questionnaire for assessing physical work loads in a general population. *J Occup Environ Med* 2002;44(8):724-35.

38. Vittinghoff E, Glidden DV, Shiboski SC, et al. Regression Methods in Biostatistics, Linear, Logistic, Survival, and Repeated Measures Models. 2nd ed. New York, USA: Springer New York 2012:395-429.

39. Hosmer DW, Lemeshow S. Applied logistic regression. 2nd ed. New York ; Chichester: Wiley 2000.

40. Steyerberg EW, Borsboom GJ, van Houwelingen HC, et al. Validation and updating of predictive logistic regression models: a study on sample size and shrinkage. *Stat Med* 2004;23(16):2567-86.

41. Schellingerhout JM, Heymans MW, Verhagen AP, et al. Prognosis of patients with nonspecific neck pain: development and external validation of a prediction rule for persistence of complaints. *Spine (Phila Pa 1976)* 2010;35(17):E827-35.

42. Kjellman G, Skargren E, Oberg B. Prognostic factors for perceived pain and function at one-year follow-up in primary care patients with neck pain. *Disabil Rehabil* 2002;24(7):364-70.

43. Verhagen AP, Karels CH, Schellingerhout JM, et al. Pain severity and catastrophising modify treatment success in neck pain patients in primary care. *Man Ther* 2010;15(3):267-72.

44. Beneciuk JM, Bishop MD, George SZ. Clinical prediction rules for physical therapy interventions: a systematic review. *Phys Ther* 2009;89(2):114-24.

45. Woodhouse A, Pape K, Romundstad PR, et al. Health care contact following a new incident neck or low back pain episode in the general population; the HUNT study. *BMC Health Serv Res* 2016;16:81.

46. Bot SD, van der Waal JM, Terwee CB, et al. Predictors of outcome in neck and shoulder symptoms: a cohort study in general practice. *Spine* 2005;30(16):E459-E70.

For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

BMJ Open: first published as 10.1136/bmjopen-2018-024557 on 24 April 2019. Downloaded from http://bmjopen.bmj.com/ on May 15, 2025 at Department GEZ-LTA Erasmushogeschool . Protected by copyright, including for uses related to text and data mining, AI training, and similar technologies.

47. Bohman T, Alfredsson L, Jensen I, et al. Does a healthy lifestyle behaviour influence the prognosis of low back pain among men and women in a general population? A population-based cohort study. *BMJ Open* 2014;4(12).

48. Svedmark A, Bjorklund M, Hager CK, et al. Impact of Workplace Exposure and Stress on Neck Pain and Disabilities in Women-A Longitudinal Follow-up After a Rehabilitation Intervention. *Ann Work Expo Health* 2018;62(5):591-603.

For peer review only

For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

BMJ Open: first published as 10.1136/bmjopen-2018-024557 on 24 April 2019. Downloaded from http://bmjopen.bmj.com/ on May 15, 2025 at Department GEZ-LTA Erasmushogeschool . Protected by copyright, including for uses related to text and data mining, AI training, and similar technologies.

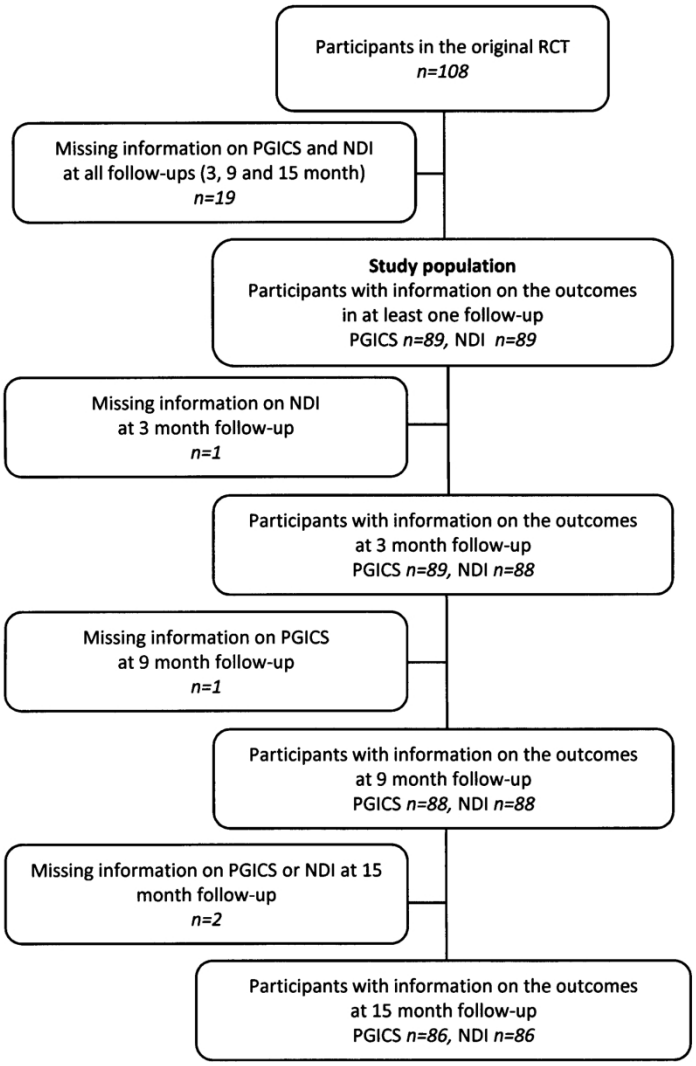

Figure 1. Included participants and progress of participants along the follow-up period concerning the outcome measures. RCT: Randomised controlled trial. PGICS: The Patient Global Impression of Change Scale. NDI: The Neck Disability Index.

206x296mm (300 x 300 DPI)

BMJ Open: first published as 10.1136/bmjopen-2018-024557 on 24 April 2019. Downloaded from http://bmjopen.bmj.com/ on May 15, 2025 at Department GEZ-LTA Erasmushogeschool . Protected by copyright, including for uses related to text and data mining, AI training, and similar technologies.

TRIPOD Checklist: Prediction Model Development

Section/Topic	Item	Checklist Item	Page
Title and abstract			
Title	1	Identify the study as developing and/or validating a multivariable prediction model, the target population, and the outcome to be predicted.	1
Abstract	2	Provide a summary of objectives, study design, setting, participants, sample size, predictors, outcome, statistical analysis, results, and conclusions.	2-3
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.	4-5
	3b	Specify the objectives, including whether the study describes the development or validation of the model or both.	5
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.	5
	4b	Specify the key study dates, including start of accrual; end of accrual; and, if applicable, end of follow-up.	5-6
Participants	5a	Specify key elements of the study setting (e.g., primary care, secondary care, general population) including number and location of centres.	5-6
	5b	Describe eligibility criteria for participants.	6
	5c	Give details of treatments received, if relevant.	NA
Outcome	6a	Clearly define the outcome that is predicted by the prediction model, including how and when assessed.	6-7
	6b	Report any actions to blind assessment of the outcome to be predicted.	NA
Predictors	7a	Clearly define all predictors used in developing or validating the multivariable prediction model, including how and when they were measured.	7 Tab 1
	7b	Report any actions to blind assessment of predictors for the outcome and other predictors.	NA
Sample size	8	Explain how the study size was arrived at.	Fig 1
Missing data	9	Describe how missing data were handled (e.g., complete-case analysis, single imputation, multiple imputation) with details of any imputation method.	6 Fig 1 Tab 2
Statistical analysis methods	10a	Describe how predictors were handled in the analyses.	12, Tab 1 Tab 3
	10b	Specify type of model, all model-building procedures (including any predictor selection), and method for internal validation.	11-13
	10d	Specify all measures used to assess model performance and, if relevant, to compare multiple models.	12-13
Risk groups	11	Provide details on how risk groups were created, if done.	NA
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.	Fig 1
	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.	13 Fig 1 Tab 2
Model development	14a	Specify the number of participants and outcome events in each analysis.	13 Tab 3 Tab 4
	14b	If done, report the unadjusted association between each candidate predictor and outcome.	Tab 3
Model specification	15a	Present the full prediction model to allow predictions for individuals (i.e., all regression coefficients, and model intercept or baseline survival at a given time point).	Tab 4
	15b	Explain how to the use the prediction model.	18 & 20-21
Model performance	16	Report performance measures (with CIs) for the prediction model.	Tab 4
Discussion			
Limitations	18	Discuss any limitations of the study (such as nonrepresentative sample, few events per predictor, missing data).	20
Interpretation	19b	Give an overall interpretation of the results, considering objectives, limitations, and results from similar studies, and other relevant evidence.	18-20

BMJ Open: first published as 10.1136/bmjopen-2018-024557 on 24 April 2019. Downloaded from http://bmjopen.bmj.com/ on May 15, 2025 at Department GEZ-LTA Erasmushogeschool . Protected by copyright, including for uses related to text and data mining, AI training, and similar technologies.

TRIPOD Checklist: Prediction Model Development

Implications	20	Discuss the potential clinical use of the model and implications for future research.	21
Other information			
Supplementary information	21	Provide information about the availability of supplementary resources, such as study protocol, Web calculator, and data sets.	22
Funding	22	Give the source of funding and the role of the funders for the present study.	22

For peer review only

BMJ Open: first published as 10.1136/bmjopen-2018-024557 on 24 April 2019. Downloaded from http://bmjopen.bmj.com/ on May 15, 2025 at Department GEZ-LTA Erasmushogeschool . Protected by copyright, including for uses related to text and data mining, AI training, and similar technologies.

BMJ Open

Predictive models for short- and long-term improvement in women under physiotherapy for chronic disabling neck pain: a longitudinal cohort study

Journal:	*BMJ Open*
Manuscript ID	bmjopen-2018-024557.R2
Article Type:	Research
Date Submitted by the Author:	30-Dec-2018
Complete List of Authors:	Bohman, Tony; Karolinska Institutet, Department of Neurobiology, Care Sciences and Society Bottai, Matteo; Karolinska Institutet, Institue of Environmental Medicine Björklund, Martin; University of Gävle, Department of Occupational and Public Health Sciences; Umeå University, Department of Community Medicine and Rehabilitation
Primary Subject Heading:	Epidemiology
Secondary Subject Heading:	Complementary medicine, Medical management
Keywords:	prediction, prognosis, non-specific neck pain, longitudinal analyses, cohort, clinical important improvement

SCHOLARONE™
Manuscripts

BMJ Open: first published as 10.1136/bmjopen-2018-024557 on 24 April 2019. Downloaded from http://bmjopen.bmj.com/ on May 15, 2025 at Department GEZ-LTA Erasmushogeschool . Protected by copyright, including for uses related to text and data mining, AI training, and similar technologies.

Predictive models for short- and long-term improvement in women under physiotherapy for chronic disabling neck pain: a longitudinal cohort study

Tony Bohman, PhD[1], Matteo Bottai, ScD[2], Martin Björklund, PhD[3, 4]

[1] Department of Neurobiology, Care Sciences and Society, Division of Physiotherapy, Karolinska Institutet, 23 100, SE-14183, Stockholm, Sweden, [2] Unit of Biostatistics, Institute of Environmental Medicine, Karolinska Institutet, Box 210, SE-17177, Stockholm, Sweden, [3] Centre for Musculoskeletal Research, Department of Occupational and Public Health Sciences, Faculty of Health and Occupational Studies, University of Gävle, Gävle, Sweden, [4] Department of Community Medicine and Rehabilitation, Physiotherapy, Umeå University, Umeå, Sweden

Corresponding author:

Tony Bohman, Department of Neurobiology, Care Sciences and Society, Karolinska Institutet, 23 100, SE-14183, Stockholm, Sweden

e-mail; tony.bohman@ki.se, cellphone; +46 70 299 62 63

Key words; prediction, prognosis, non-specific neck pain, neck pain, longitudinal analyses, cohort, clinical important improvement, discrimination

Word count: 3944

Figures: 1

Tables: 4

References: 48

Supplementary files: 0

For peer review only

Protected by copyright, including for uses related to text and data mining, AI training, and similar technologies.

Erasmushogeschool .

ABSTRACT

Objectives

To develop predictive models for short- and long-term clinically important improvement in women with non-specific chronic disabling neck pain during the clinical course of physiotherapy.

Design

Longitudinal cohort study based on data from a randomized controlled trial evaluating short- and long-term effects on sensorimotor function over eleven weeks of physiotherapy.

Participants and settings

Eighty-nine women aged 31-65 years with non-specific chronic disabling neck pain from Gävle, Sweden.

Measures

The outcome, clinically important improvement, was measured with the Patient Global Impression of Change Scale (PGICS) and the Neck Disability Index (NDI), assessed by self-administered questionnaires at 3, 9 and 15 months from the start of the interventions (baseline). Twelve baseline prognostic factors were considered in the analyses. The predictive models were built using random-effects logistic regression. The predictive ability of the models was measured by the area under the receiver operating characteristic curve (AUC). Internal validity was assessed with cross-validation using the bootstrap resampling technique.

Results

Factors included in the final PGICS-model were neck disability and age, and in the NDI-model, neck disability, depression and catastrophizing. In both models the odds for short- and long-term improvement increased with higher baseline neck disability, while the odds decreased with increasing age (PGICS-model), and with increasing level of depression (NDI-model). In the NDI-model, higher baseline levels of catastrophizing indicated increased odds for short-term improvement and decreased

For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

For peer review only

Protected by copyright, including for uses related to text and data mining, AI training, and similar technologies.

Erasmushogeschool .

odds for long-term improvement. Both models showed acceptable predictive validity with an AUC of 0.64 (95% CI; 0.55-0.73) and 0.67 (95% CI; 0.59-0.75), respectively.

Conclusion

Age, neck disability and psychological factors seems to be important predictors of improvement, and may inform clinical decisions about physiotherapy in women with chronic neck pain. Before using the developed predictive models in clinical practice, however, they should be validated in other populations and tested in clinical settings.

Article summary

Strengths and limitations of this study

- Strengths of this study are a well-defined sample and thorough development of predictive models.
- The longitudinal design with a short- and long-term follow-up time, and the inclusion of biopsychosocial prognostic factors in the analyses further strengthens the study.
- A limitation of this study is the relatively small sample.

For peer review only

Protected by copyright, including for uses related to text and data mining, AI training, and similar technologies. Erasmushogeschool .

INTRODUCTION

Neck pain is a common health problem and a cause of substantial disability which has a considerable social and economic impact throughout the world.[1] Hogg-Johnson et al. estimated the 12-month prevalence of neck pain to range between 30% and 50%, with a higher prevalence among women.[1] The prevalence of neck pain has increased during the last decades, and in 2015 neck and low back pain were the leading causes of disability.[2 3] Neck pain often is unrelated to any other specific pathology.[4] Although single episodes of neck pain generally dissolve over time, they are likely recurrent and may become chronic.[5] In a review from 2008 Carroll et al. concluded that 50% to 85% of persons with neck pain do not experience complete resolution of their pain.[5]

Prognostic research can help understand the course and future outcome in individuals with neck pain.[6] Guzman et al. summarised the work of the 2000-2010 Neck Pain Task Force concluding that younger age, no previous pain, good physiological and psychological health, good coping, good social support, exercise and sports, and no prior sick leave may increase the chance of recovery from neck pain.[7] Walton et al. surveyed prognostic factors for prolonged recovery from neck pain in 13 systematic reviews.[8] They found evidence only for past history of musculoskeletal disorders and older age to prolong recovery in non-whiplash related neck pain. For the remaining factors evaluated there was insufficient evidence for the influence on neck pain, and more research was recommended.

Neck-pain patients commonly seek physical therapy, but predicting treatment outcome and prognosis for these patients is challenging.[9] Predictive models based on multiple prognostic factors could guide healthcare providers, such as physiotherapists, in determining which patients are more likely to improve and to help all patients develop informed expectations.[10 11] It is generally recommended to build predictive models that are applicable to a well-defined patient population and the healthcare system.[10] Women have a higher risk of chronic neck pain than men, and it has been suggested that women should be assessed separately from men in prognostic research.[12 13] Using the search strategy for predictive models in physiotherapy and musculoskeletal complaints suggested by van Oort et al., we found only one study assessing chronic non-specific neck pain, and none with a model specific for women.[14 15]

For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

Protected by copyright, including for uses related to text and data mining, AI training, and similar technologies.
Erasmushogeschool .

The individual perception of pain and disability vary during the course of an episode, and the effect of prognostic factors is therefore expected to change over time following physiotherapy.[15 16] The analysis of longitudinal data is effective in evaluating these potential changes over time, as it can separate the change between individuals from that within any given patient. Longitudinal analyses have been recommended in prospective cohort studies on musculoskeletal problems.[17 18] The aim of this study was to develop predictive models for short- and long-term clinically important improvement in women with chronic disabling neck pain in the clinical course of physiotherapy.

METHODS

Design and study population

This longitudinal cohort study sought to develop predictive models, including multiple prognostic factors jointly, for chronic neck pain in women. Predictive models are one of the four themes of the Prognosis Research Strategy Framework for Prognostic Studies.[6 11] Carroll et al. classify predictive models as "Phase II" studies in a 3-level hierarchy of evidence from longitudinal studies, and suggests them suitable for predicting recovery from neck pain.[5]

We used data from a randomized control trial (RCT) evaluating the short- and long-term effects, following eleven weeks of physiotherapy interventions (coordination exercise, strength training and massage), on sensorimotor function in 108 women with non-specific chronic disabling neck pain.[19] The trial was carried out in Gävle, Sweden, in 2008 and was approved by the ethics review board in Uppsala, Sweden. Participants gave their written consent to participate in the RCT.

The RCT included Swedish-speaking women aged 25 to 65 years with non-specific disabling neck pain lasting for 3 months or more (chronic). The women were recruited via the social insurance agency and with advertisement in local papers and invitations at municipality and county council work sites, primary and occupational healthcare units. Non-specific chronic disabling neck pain was defined as neck pain reported by the patient as the "most painful area" along with disability, measured as > 9 normalised points of the first 19 items in the Disability Arm Shoulder Hand questionnaire

For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

Protected by copyright, including for uses related to text and data mining, AI training, and similar technologies. Erasmushogeschool .

(DASH).[20 21] These 19 items refer to disability in activities of daily living regarding neck, shoulders and arms. Excluded were individuals with trauma to the head or neck, a diagnosis of rheumatic, neurological, connective tissue, inflammatory or endocrine disease or psychiatric diagnosis affecting their everyday life, fibromyalgia, cancer, stroke, cardiac infarction, diabetes types I, cervical radiculopathy, vestibular disorders, surgery or fracture to the back, neck, or shoulder in the last 3 years or shoulder luxation in the last year. Finally, strenuous exercise more than 3 times per week during the previous 6 months also led to exclusion.[19]

Patient and Public Involvement

As this study was based on secondary data from a RCT, patients were not directly involved in the design and completion of the study.

Data collection and variables

Before the start of the intervention (baseline), participants filled in a self-administered questionnaire, containing instruments and questions to measure the potential prognostic factors. Outcome information was collected by follow-up questionnaires at three, nine and 15 months from baseline. Participants who did not provide information on the outcome at any of the three follow-ups were excluded, resulting in a study population of 89 participants (Figure 1).

Figure 1

Outcome

The Patient Global Impression of Change Scale (PGICS) provided information for the outcome "global perceived change of general health" by comparing general health at follow-up with general health at baseline. PGICS is a 7-point ordinal Likert scale (very much improved, much improved, minimally improved, not changed, minimally worse, much worse and very much worse).[22] The scale categories were dichotomized into "improved" (very much improved, much improved) and "not improved" (all the other categories). According to the IMMPACT recommendations for clinical important outcomes in chronic pain, the 7- point scale is recommended when assessing general health. The categories "very much improved" and "much improved" reflects what patients consider to be a

For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

Protected by copyright, including for uses related to text and data mining, AI training, and similar technologies. Erasmushogeschool .

clinical important improvement in general health.[23] The Neck Disability Index (NDI) provided information for the second outcome.[24] The NDI has 10 items (pain intensity, personal care, lifting, reading, headaches, concentration, work, driving, sleeping and recreational activities) with 6 possible answers in each item, scored 0 (no limitation) to 5 (major limitations). Total score of the NDI range from 0 to 50. The NDI has high reliability, strong internal consistency and strong validity, when compared with other instruments for evaluating patients with neck pain.[24] In the present study we used the normalised NDI (NDI %, 0-100). The minimal important change (MIC) for the NDI % was set equal to 6.3.[25] Using MIC as a cut-off, a dichotomized NDI outcome was constructed for each follow-up, where a clinical important improvement was defined as a NDI % decrease of more than 6.3 between the baseline and the follow-up, and "no improvement" as an increase, or a decrease less than or equal to 6.3 NDI %. Participants with a NDI % of 0 at follow-up were also defined as having a clinical important improvement regardless of the baseline score.

Potential prognostic factors

The selection of potential prognostic factors was based on systematic reviews and prospective studies on the prognosis of non-specific neck pain, clinical considerations and availability in the data (Table 1). Eight potential prognostic factors had support from literature; age, neck disability, average pain intensity, depression, fear of movement, catastrophizing, social support and leisure physical activity.[5 8 26 27] Chronic widespread pain, recovery expectation, physical work load and dual-working were considered potential prognostic factors based on clinical considerations.

For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

Protected by copyright, including for uses related to text and data mining, AI training, and similar technologies. Erasmushogeschool .

Table 1. Potential prognostic factors and corresponding bibliographical references to definition and psychometric properties of the factors.

Potential prognostic factor	Measurement	Categorisation in the analyses
Age	Age at baseline	Continuous
Neck disability[24]	Normalised Neck Disability Index (NDI%)	Continuous, 1-100 0 = "no disability" and 100 = "complete disability"
Average pain intensity[28]	Average pain intensity during the previous week measured on an 11-point Numeric Rating Scale (NRS)	Continuous, 0-10 0 = "no pain" and 10 = "pain as bad as it could be"
Depression[29]	Self-rating version of the Montgomery Åsberg Depression Rating Scale (MADRS-S)	Continuous, 0-54 0 = "no depressive symptoms" and 54 = "severe depression"
Fear of movement[30 31]	The Tampa scale of kinesiophobia	Continuous, 17-68. A sum score of 17-68 were higher score indicate higher fear of movement
Catastrophizing[32]	The six item catastrophizing subscale from the Coping Strategies Questionnaire (CSQ).	Continuous, 0-36 Each item of the subscale had a score of 0-6 were a high score indicated a high degree of catastrophizing
Social support[33]	Item number 5 and 14 of the Swedish Multidimensional Pain Inventory (MPI-S)	Continuous, 1-12 Each item with a score of 0-6, where 0 = "no social support" and 12 = "high social support"

For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

For peer review only

Protected by copyright, including for uses related to text and data mining, AI training, and similar technologies.

Erasmushogeschool . http://bmjopen.bmj.com/ on May 15, 2025 at Department GEZ-LTA

136/bmjopen-2018-024550 on 24 April 2019. Downloaded from

Recovery expectation[34]	The answer to the question; "Do you think that any intervention or exercise will lead to recovery?"	Continuous, 1-5 5 point ordinal Likert scale from 1 = "No, definitely not" to 5 = "Yes, completely recovered"
Chronic widespread pain[35]	Derived from a pain drawing	Yes; pain in all 4 quadrants of the body together with spinal pain
Leisure physical activity[36]	"How much have you, in general, moved or exerted yourself physically during leisure time in the past year"	- No/low intensity; very little/an occasional walk or similar/ every day physical activity like gardening, cleaning/low intensity physical activity e.g. walking or similar at least once a week - Moderate/high intensity; more strenuous physical activity e.g. jogging, swimming etc. at least once a week/regular high intensity physical activity e.g. running, ball sports etc.
Physical workload[37]	"How physically strenuous has your work or daily activity been the past 12 months?"	- Mostly sedentary - Low/heavy workload; low physical work load but mobile/quite physical, strenuous work/physically strenuous work

For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

For peer review only

136/bmjopen-2018-024557 on 24 April 2019. Downloaded from http://bmjopen.bmj.com/ on May 15, 2025 at Department GEZ-LTA Erasmushogeschool Brussel. Protected by copyright, including for uses related to text and data mining, AI training, and similar technologies.

Dual-working	A combination of three items; 1) Working/not working. 2) What does your household look like? 3) Who is primarily responsible for and performing the housework in your family?	- Yes; 1) working, 2) living together with children and/or another adult person and 3) having the responsibility for the housework - No; any other combination of the three items (see the method section)

For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

For peer review only

bmjopen-2018-024557 on 24 April 2019. Downloaded from http://bmjopen.bmj.com/ on May 15, 2025 at Department GEZ-LTA Erasmushogeschool . Protected by copyright, including for uses related to text and data mining, AI training, and similar technologies.

Average pain intensity was not limited to neck pain, but all participants reported neck pain as the "most painful area", as this was a criterion for inclusion in the RCT.[19] Dual-working was a combination of three items: 1) Working/not working, 2) What does your household look like? (living alone, living alone with children, living with another adult, living with another adult and children), 3) Who is primarily performing the housework in your family? (myself, someone else, equally shared). The factor dual-working was then dichotomized according to the answers into; yes (working, living with children and/or another adult, and performing the housework) and no (any other combination of the three items). Dual-working has to our knowledge not been evaluated in previous studies, but in our opinion it is possibly associated with the prognosis of neck pain in women.

Statistical methods

Descriptive statistics are presented as means and standard deviations (SD) or median and interquartile range (IQR) when appropriate. The level of the confidence intervals (CI) was set at 95% and that of the tests at 5%. All p-values were two-sided. Stata version 14.2 (StataCorp College Station, TX, USA) was used in the analyses.

Random-effects logistic regression models were used to estimate the probability of a clinically important improvement of the outcomes from baseline to three and 15-months follow-up.[17] Data from all three follow-ups, three, nine and 15-months, were used in the analyses. Random-effects logistic regression can model longitudinal data efficiently, while taking into account the potential dependence of the repeated measures taken on each participant.[17] The regression models were estimated for each of the two outcomes, PGICS and NDI, separately. Both outcomes showed strong associations between the follow-ups. The linearity of the relationship between the logit of the probability of the outcome variables and numeric independent variables (potential prognostic factors) was verified by means of restricted cubic splines.[17 38] None of the numeric independent variables showed evidence against linearity.

Random-effects logistic regressions, including data from all three follow-ups, were used for all potential prognostic factors one at a time to estimate the time-specific odds ratios (OR) with 95% CI for each of the two outcome measures, separately. If the interaction term (factor-by-time) was not

For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

Protected by copyright, including for uses related to text and data mining, AI training, and similar technologies. Erasmushogeschool .

statistically significant, the analyses were repeated without the interaction term. This resulted in a single OR for the factor from three to 15 months. When the interaction was significant, the OR at three and 15 months were reported separately. Potential prognostic factors with a p-value ≤ 0.2 for the estimated OR were considered candidate factors for the predictive models.[38] Based on an a priori decision of clinical relevance, statistical effect measure modifications were tested between pain intensity and depression or recovery expectations. If the effect measure modification was statistically significant, this was included in the subsequent analyses.[38 39]

Developing the models

A sequential backward manual selection procedure with the random-effects logistic regressions was used to build the predictive models.[38] All candidate factors were included in the initial model. The factor with the highest p-value (Wald-test) were excluded one by one until all factors in the model had a p-value ≤ 0.1.[38] If a candidate factor showed effect-modification with time, then the factor was included together with the effect measure modification in the model. During the development process, all the analyses were adjusted for the assigned RCT interventions. "Intervention" was then removed from the final predictive models before evaluating the models and presenting the results. The association between the prognostic factor and the outcome was reported as beta-coefficient (β) with standard error (SE), OR with 95% CI and associated p-value.

Evaluation of the models

The bias corrected area under the receiver operating characteristic curve (AUC) with 95% CI was obtained by cross-validation based on 100 design-matrix bootstrap replicates and used to determine the internally-validated predictive ability of the models.[38 39] The AUC represents a summary of the sensitivity and specificity of the model in distinguishing participants who improve during the follow-up period from those who do not. The AUC ranges from 0.5 (no predictive ability) to 1.0 (perfect predictive ability). Overfitting was assessed by calculating the heuristic shrinkage factor.[40] A shrinkage factor of 1.0 indicates no overfitting of the model. The shrinkage corrected beta-coefficients (Sβ) were calculated by the formula; shrinkage factor x β.

For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

Protected by copyright, including for uses related to text and data mining, AI training, and similar technologies.
Erasmushogeschool .

Sensitivity analyses

To compare the study population with that of the non-responders, we used the chi-squared test for categorical variables, and the t-test or the Wilcoxon's rank-sum test for continuous variables.

RESULTS

Study population

Baseline characteristics of the study population are listed in Table 2. The women's age ranged between 31 and 65 years, and all women reported neck pain duration of more than eight months, with a median of 120 months (IQR 60-216). Eighty women (91%) were working and 66 (74%) reported no sick leave because of neck pain during the previous 6 months. Using PGICS as outcome measure 47 (53%) women were categorised as improved at 3-month, 31 (35%) at 9-month and 26 (30%) at 15-month follow-up while using NDI as outcome measure 39 (44%) women had improved at 3 months, 37 (42%) at 9 months and 31 (36%) at 15 months. Only one participant reported "no neck disability" (NDI% = 0) at the three and 15-month follow-up, respectively, while none reported "no neck disability" at the 9-month follow-up.

Table 2. Baseline characteristics of the study population, n=89.

Characteristics			Missing (n)[a]
Age median (IQR)	52	(47-59)	0
Neck disability median (IQR)	28	(20-33)	0
Average pain intensity mean (SD)	5.2	(1.6)	0
Depression median (IQR)	8	(6-12)	1
Fear of movement median (IQR)	29	(26-33)	0
Catastrophizing median (IQR)	6	(3-11)	0
Social support mean (SD)	6.2	(3.4)	1
Recovery expectation median (IQR)	4	(3-4)	4
Chronic widespread pain freq (%)			0

For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

Protected by copyright, including for uses related to text and data mining, AI training, and similar technologies. Erasmushogeschool .

Yes	40	(45)	
Leisure physical activity freq (%)			0
No/low intensity	60	(67)	
Moderate/high intensity	29	(33)	
Physical workload freq (%)			1
Mostly sedentary	36	(41)	
Low/heavy work load	52	(59)	
Dual-working freq (%)			4
Yes	38	(45)	

[a] missing answer, IQR; interquartile range, SD; standard deviation, freq; frequency.

Development and evaluation of the predictive model

The analyses on each potential prognostic factor are presented in Table 3. The follow-up data observations used for the analyses differed slightly between the two outcome measures because of missing responses (Figure 1). No effect measure modification was observed between pain intensity and depression or recovery expectations. In the analyses with PGICS as outcome measure age, neck disability, and average pain intensity met the criteria for inclusion into the predictive model analysis. No potential prognostic factor appeared to modify the effect of time. In the corresponding analyses with NDI as outcome measure, five potential prognostic factors met the criteria for inclusion: age, neck disability, depression, catastrophizing, and leisure physical activity. The effect of catastrophizing changed over time, why an effect measure modification term (catastrophizing x time) was added to the predictive model analysis.

Table 3. Random-effects regression analyses* for potential short- and long-term prognostic factors with PGICS and NDI as outcome, n=89.

Potential prognostic factor	PGICS				
	n/obs[a]	OR 3–15 m[b]	95% CI	p-value	p-eff.m.[c]
Age	*89/263*	0.92	0.84, 1.01	0.08	0.75

For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

Protected by copyright, including for uses related to text and data mining, AI training, and similar technologies.

Erasmushogeschool .

Neck disability	*89/263*	1.08	1.01, 1.16	0.03	0.26
Average pain intensity	*89/263*	1.60	1.00, 2.55	0.05	1.00
Depression	*88/260*	1.04	0.92, 1.19	0.50	0.07
Fear of movement	*89/263*	0.98	0.87, 1.09	0.67	0.48
Catastrophizing	*89/263*	1.06	0.94, 1.20	0.34	0.20
Social support	*88/260*	1.08	0.88, 1.33	0.47	0.57
Recovery expectations	*85/253*	1.74	0.71, 4.25	0.22	0.47
Chronic widespread pain	*89/263*				0.45
No		1.0			
Yes		1.99	0.46, 8.66	0.36	
Leisure physical activity	*89/263*				0.36
No/low intensity		1.0			
Moderate/high intensity		0.77	0.16, 3.65	0.75	
Physical workload	*88/260*				0.64
Mostly sedentary		1.0			
Low to heavy workload		1.35	0.31, 5.86	0.69	
Dual-working	*85/251*				0.41
No		1.0			
Yes		0.77	0.17, 3.39	0.73	

Potential prognostic factor	**NDI**				
	***n/obs*[a]**	**OR 3–15 m[b]**	**95% CI**	**p-value**	**p-eff.m.[c]**
Age	89/262	0.96	0.90, 1.02	0.20	0.68
Neck disability	89/262	1.05	1.01, 1.11	0.02	0.31
Average pain intensity	89/262	1.17	0.84, 1.63	0.35	0.67
Depression	88/259	0.94	0.86, 1.03	0.17	0.75
Fear of movement	89/262	0.99	0.92, 1.07	0.87	0.88
Catastrophizing	89/262				0.03
3 m[d]		1.10	0.98, 1.24	0.12	

For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

Protected by copyright, including for uses related to text and data mining, AI training, and similar technologies.

15 m[e]		0.93	0.83, 1.05	0.23	
Social support	88/259	1.08	0.93, 1.26	0.32	0.72
Recovery expectations	85/253	0.73	0.39, 1.37	0.33	0.37
Chronic widespread pain	89/262				0.10
No		1.0			
Yes		0.72	0.26, 1.99	0.53	
Leisure physical activity	89/262				0.36
No/low intensity		1.0			
Moderate/high intensity		0.48	0.16, 1.43	0.19	
Physical workload	88/259				0.06
Mostly sedentary		1.0			
Low to heavy workload		1.16	0.41, 3.25	0.78	
Dual-working	85/250				0.16
No		1.0			
Yes		0.55	0.19, 1.58	0.27	

* Data from all three follow-ups (3, 9 and 15 month) were used in the analyses.

OR=odds ratio, an OR>1 reflects a higher odds of clinical important improvement and an OR<1 reflects a lower odds of clinical important improvement, Potential prognostic factors included in the development of the predictive models are presented in italics, PGICS: Patient Global Impression of Change Scale, NDI: normalised Neck Disability Index, [a] number of participants in the analyses/number of outcome observations in the analyses, [b] odds ratios for clinically important improvement between 3 to 15 months, CI: Confidence interval, [c] p-value for the effect modification over time between 3 to 15 months from baseline, [d and e] results (OR, 95% CI and p-values) for clinically important improvement at 3 and 15 months respectively.

The resulting predictive models from the sequential selection procedure are presented in Table 4. Internal validation showed acceptable predictive ability for the models of 0.64 and 0.67 respectively (Table 4). The calculated shrinkage factor was 0.73 for the PGICS-model and 0.65 for the NDI-model.

For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

Protected by copyright, including for uses related to text and data mining, AI training, and similar technologies.
Erasmushogeschool .

Table 4. The final predictive models* of clinically important improvement in chronic disabling neck pain with PGICS and NDI as outcome.

Prognostic factor	PGICS *(89/263)[a]*					
	β	**SE**	**OR**	**95% CI**	**p-value**	**Sβ**
Neck disability	0.08	0.04	1.08	1.01, 1.16	0.03	0.06
Age	-0.08	0.05	0.92	0.84, 1.01	0.08	-0.06
AUC (95% CI)[c]	0.64 (0.55, 0.73)					
Prognostic factor	**NDI** *(88/259)[a]*					
	β	**SE**	**OR**	**95% CI**	**p-value**	**Sβ**
Neck disability	0.08	0.03	1.08	1.02, 1.14	0.01	0.05
Depression	-0.11	0.05	0.89	0.81, 0.98	0.02	-0.07
Catastrophizing						
3 months	0.07	0.06	1.08	0.96, 1.21	0.21	0.05
15 months	-0.09	0.06	0.92	0.82, 1.03	0.14	-0.06
x time[b]	-0.01	0.01	0.99	0.97, 1.00	0.03	-
AUC (95% CI)[c]	0.67 (0.59, 0.75)					

* Data from all three follow-ups (3, 9 and 15 month) were used in the models.

The intercept (β_0) for the PGICS-model was; 1.27, and for the NDI-model; -1.89.

OR=odds ratio, an OR>1 reflects a higher odds of clinical important improvement and an OR<1 reflects a lower odds of clinical important improvement, PGICS: Patient Global Impression of Change Scale, NDI: normalised Neck Disability Index, β: beta-coefficient, SE: standard error, CI: confidence interval, Sβ: shrinkage corrected beta-coefficient (shrinkage factor x β), [a] number of participants in the analysis/number of outcome observations in the analysis, [b] effect measure modification term in the model; catastrophizing x time, [c] internally validated receiver operating characteristics curve (AUC) with 95% CI.

Sensitivity analyses

For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

Protected by copyright, including for uses related to text and data mining, AI training, and similar technologies. Erasmushogeschool .

Non-responders (n = 19) showed no statistically significant differences in the characteristics from the study population except for average pain intensity, where non-responders had a higher median of 6.5 compared with a median of 5 (p = 0.03) in the study population.

DISCUSSION

We developed and internally validated predictive models for clinically important short- and long-term improvement from chronic disabling neck pain among women in the clinical course of physiotherapy. The models were developed for the "global perceived change of general health" (PGICS) and the Neck Disability Index (NDI), separately. Both models had acceptable predictive ability.[39] The results showed that, when assessing potential biopsychosocial prognostic factors, perceived disabilities related to neck pain, depression, catastrophizing and age are of importance for predicting short- and long-term improvements in these women. Further, we found that prognostic factors could predict different results depending on the follow up time, as for catastrophizing in the NDI-model. This is important in the management of patients in clinical settings. Similarly to previous studies, we found that the prognostic factors in the models could differ depending on the outcome.[16 34]

Our results indicate that the odds for clinically important improvement, with PGICS as outcome measure, decrease with age and increase with higher baseline levels of disability related to neck pain. With NDI as an outcome measure, the odds for improvement increased with higher baseline levels of neck pain-related disability and decrease with higher levels of depression. These results were valid over the total follow up time of 15 months. However, the NDI-model indicated increased odds for short-term improvement, but decreased odds for long-term improvement with higher levels of catastrophizing at baseline. This interesting finding was made possible by the longitudinal nature of our study design. To the best of our knowledge, this is the first study using longitudinal analyses in predictive models for neck pain. Interestingly, depression was found to be a predictor even though women with a psychiatric diagnosis affecting their everyday life were excluded from the study.

The relative strength of the incorporated factors in the model should be interpreted with great caution as their independent effect on the outcome were not thoroughly examined.

For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

Protected by copyright, including for uses related to text and data mining, AI training, and similar technologies.
Erasmushogeschool .

Our findings are somewhat different from those of other similar studies, because of the different study populations, potential prognostic factors examined, outcomes and follow up times. We found only one prediction study on patients with chronic non-specific neck pain in physiotherapy, but with a study population also including males.[15] Poor outcome was predicted by pain medication at discharge and at one-year follow-up, and by catastrophizing at one-year follow-up, the latter in line with our results. Similarly to our study, the outcome was assessed as a minimal clinical important difference, but was based on the Northwick neck pain questionnaire.

We found four reports on non-specific neck pain predictive models with reasonably similar outcomes, methods and follow-up time as in the present study.[34 41-43] However, all four reports included both male and female patients with different durations of pain (acute, subacute and chronic), and were not performed in the course of physiotherapy only. Similarly to us, Hill et al. and Verhagen et al. found the psychological factors catastrophizing and depression/distress to predict their outcomes.[34 43] Also, baseline neck disability was included in the models by Hill et al. and by Kjellman et al.[34 42] Other factors in their models were; pain intensity, treatment expectations, concomitant back pain, manual social class, well-being and somatisation, while we found that treatment expectations and pain intensity were not important predictors in our study.[34 42 43] Shellingerhout et al. presented a predictive model with a set of nine predictors for global perceived recovery in an adult primary care population.[41] With the exception of age, none of the predictors found were similar to our predictors, a discrepancy that may be explained by different study settings, population and outcome compared with our study. In their population only 34% reported chronic neck pain and 60% were women. Further, only 28% of the patients were referred to physiotherapy while the others were referred to "usual care", spinal manipulation or a behaviour graded activity program. Even though Shellingerhout et al. reported a model including nine predictors, their predictive ability (AUC = 0.66) was similar to that of our models (AUC of 0.64 and 0.67). One could speculate that as prognostic factors in research related to neck pain most often are weak, reaching higher levels of predictive ability may be hard even with large samples and well conducted analyses.[5 8]

For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

Protected by copyright, including for uses related to text and data mining, AI training, and similar technologies. Erasmushogeschool .

Our study meets most of the important criteria for deriving predictive models in relation to musculoskeletal disorders and physiotherapy suggested by Beneciuk et al.: a well-defined study population, longer follow-up times than six months and psychological and psychosocial assessments incorporated in the model-development.[44] Other strengths of our study are a follow-up rate of 82% and a small number of missing data. We used longitudinal analyses, an advantage when assessing individual change over time.[18] The outcome, clinical important improvement, was based on the IMMPACT recommendations (PGICS), and on responsiveness analyses in which the same sample as in the present study was included (NDI).[23 25] The use of conservative "cut-points" for the Wald test in the selection procedure in order to decrease the risk of type II errors, are also supported in literature.[38 39]

Our study also has limitations. The sample size of 89 participants could be considered small when conducting a prediction study. A small sample size increases the risk of over-dispersion during analyses. However, the sample size was large enough to ensure the recommendations of 10 to 15 participants for each parameter estimate (coefficient) included in the analyses.[38 44] Furthermore, our results are based on secondary analyses of data, possibly limiting information on additional prognostic factors which could have influenced the derivation of the models. Of the 108 women included at baseline, 19 did not respond to any of the three follow-ups and were excluded from the analyses. They showed similar characteristics as the included women except for an average pain intensity with a median of 6.5 compared with a median of 5 in the study population. Therefore, attrition might have influenced the results. Some of the participants were recruited by advertisement and could have different characteristics than ordinary healthcare patients.[45] However, the baseline levels of average pain intensity, neck pain-related disability and fear of movement in the study were similar to those in the study by Shellingerhout et al., who investigated prognostic factor for neck pain in a sample of patients referred to primary care.[41]

The clinical implication of our study findings is that baseline neck disability seems to be an important factor to consider, as a higher baseline disability was associated with higher odds for clinical important improvement in both our models. This is in line with the findings of Bot et al. in exploring

For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

Protected by copyright, including for uses related to text and data mining, AI training, and similar technologies.
Erasmushogeschool .

predictors for patients with neck or shoulder pain in general practice.[46] They found, that being more disabled at baseline predicted a larger reduction in disability at 3 and 12-month follow-up. Furthermore, psychological factors are important to consider in the clinical course of physiotherapy concerning women with chronic neck pain. As psychological factors are modifiable they may be targeted in order to increase the possibility for short- and long-term improvement in the management of these women. The information about the prognostic factors and the outcomes included in our models is easily collected at the first consultation by a physiotherapist, and the models could be a valuable tool to help physiotherapists manage these patients.

While the predictive ability of our models was acceptable, it also indicated that there may still be other factors that could help predict the outcome more precisely. It would therefore be valuable to include variables in future investigations that were not included in the present study, like for example lifestyle factors such as tobacco and alcohol use, and psychological factors related to work.[47 48] Our models will make clinicians aware of what factors are important to consider when predicting which patients will have the best chance of a clinical important improvement. Also notable to clinicians is that factors can vary depending on the outcome measured, and that the chance of improvement can change over time for some factors, as for catastrophizing in the current study. Furthermore, our results facilitate future prognostic research related to chronicity in neck pain. A predictive model development, including internal validation, is only the first step in the process of deriving a model that could be implemented in clinic. A second step should be external validation, for example, by using data from RCTs including other types of interventions targeting chronic neck pain. Finally, further external validation should be done by investigating the impact of the model in clinical practice before implementation.[11] Because all women in our sample underwent physiotherapy, our predictive models should be restricted to this population and setting. The validity in other populations and other healthcare providers will remain unknown until external validations will be available.

CONCLUSION

For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

Protected by copyright, including for uses related to text and data mining, AI training, and similar technologies. Erasmushogeschool .

The developed predictive models evaluating clinical important improvement from chronic non-specific neck pain among women in the clinical course of physiotherapy showed acceptable predictive ability. Age, neck pain-related disability, depression, and catastrophizing seems to be factors that can be of guidance for physiotherapists trying to predict short- and long-term clinical important improvement in these patients. With the exception of neck pain-related disability, the different outcome measures had different sets of prognostic factors. The effect of some factors may be modified by time. The present study is the first step towards developing predictive models for clinical practice. The next steps will include external validations in different neck pain populations and clinical settings.

Author contributions: T Bohman, M Björklund and M Bottai contributed to the design of the study. T Bohman made the statistical analyses supported by M Bottai and wrote the first manuscript version. All authors contributed to the interpretation of the data and critically revised all versions of the manuscript and finally approved the last version.

Acknowledgements:

We thank Maria Frykman and Thomas Rudolfsson for excellent administration and data acquisition.

Funding:

The study was funded by Alfta Research Foundation, grants from the Swedish Council for Working Life and Social Research (2006-1162), Länsförsäkringar Forskning och Framtid (51-1010/06) and Forte Centre Working Life "The body at work – from problem to potential" (2009-1761).

Competing interests: None declared.

Ethical approval: The ethics review board in Uppsala, Sweden, approved the study (Registration nr. 207/206).

Data sharing: No additional data available.

For peer review only

Protected by copyright, including for uses related to text and data mining, AI training, and similar technologies.
Erasmushogeschool .

Transparency: The corresponding author (T Bohman) affirms that the manuscript is an honest, accurate, and transparent account of the study being reported; that no important aspects of the study have been omitted; and that any discrepancies from the study as planned have been explained.

Figure 1. Included participants and progress of participants along the follow-up period concerning the outcome measures. RCT: Randomised controlled trial. PGICS: The Patient Global Impression of Change Scale. NDI: The Neck Disability Index.

REFERENCES

1. Hogg-Johnson S, van der Velde G, Carroll LJ, et al. The burden and determinants of neck pain in the general population: results of the Bone and Joint Decade 2000-2010 Task Force on Neck Pain and Its Associated Disorders. *Spine (Phila Pa 1976)* 2008;33(4 Suppl):S39-51.
2. Vos T, Allen C, Arora M, et al. Global, regional, and national incidence, prevalence, and years lived with disability for 310 diseases and injuries, 1990–2015: a systematic analysis for the Global Burden of Disease Study 2015. *The Lancet* 2016;388(10053):1545-602.
3. Hoy D, March L, Woolf A, et al. The global burden of neck pain: estimates from the global burden of disease 2010 study. *Ann Rheum Dis* 2014;73(7):1309-15.
4. The burden of musculoskeletal conditions at the start of the new millennium. World Health Organ Tech Rep Ser 2003;919:i-x, 1-218, back cover.
5. Carroll LJ, Hogg-Johnson S, van der Velde G, et al. Course and prognostic factors for neck pain in the general population: results of the Bone and Joint Decade 2000-2010 Task Force on Neck Pain and Its Associated Disorders. *Spine* 2008;33(4 Suppl):S75-82.
6. Hemingway H, Croft P, Perel P, et al. Prognosis research strategy (PROGRESS) 1: a framework for researching clinical outcomes. *BMJ* 2013;346:e5595.
7. Guzman J, Haldeman S, Carroll LJ, et al. Clinical practice implications of the Bone and Joint Decade 2000-2010 Task Force on Neck Pain and Its Associated Disorders: from concepts and findings to recommendations. *Spine* 2008;33(4 Suppl):S199-213.

For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

Protected by copyright, including for uses related to text and data mining, AI training, and similar technologies. Erasmushogeschool .

8. Walton DM, Carroll LJ, Kasch H, et al. An Overview of Systematic Reviews on Prognostic Factors in Neck Pain: Results from the International Collaboration on Neck Pain (ICON) Project. *The Open Orthopaedics Journal* 2013;7:494-505.

9. Hurwitz EL, Carragee EJ, van der Velde G, et al. Treatment of neck pain: noninvasive interventions: results of the Bone and Joint Decade 2000-2010 Task Force on Neck Pain and Its Associated Disorders. *J Manipulative Physiol Ther* 2009;32(2 Suppl):S141-75.

10. Beattie P, Nelson R. Clinical prediction rules: what are they and what do they tell us? *Aust J Physiother* 2006;52(3):157-63.

11. Steyerberg EW, Moons KG, van der Windt DA, et al. Prognosis Research Strategy (PROGRESS) 3: prognostic model research. *PLoS Med* 2013;10(2):e1001381.

12. Bohman T, Alfredsson L, Hallqvist J, et al. The influence of self-reported leisure time physical activity and the body mass index on recovery from persistent back pain among men and women: a population-based cohort study. *BMC Public Health* 2013;13(1):385.

13. Messing K, Stock SR, Tissot F. Should studies of risk factors for musculoskeletal disorders be stratified by gender? Lessons from the 1998 Quebec Health and Social Survey (vol 35, pg 96, 2009). *Scand J Work Env Hea* 2009;35(5):400-00.

14. van Oort L, van den Berg T, Koes BW, et al. Preliminary state of development of prediction models for primary care physical therapy: a systematic review. *J Clin Epidemiol* 2012;65(12):1257-66.

15. Cecchi F, Molino-Lova R, Paperini A, et al. Predictors of short- and long-term outcome in patients with chronic non-specific neck pain undergoing an exercise-based rehabilitation program: a prospective cohort study with 1-year follow-up. *Intern Emerg Med* 2011;6(5):413-21.

16. Pool JJ, Ostelo RW, Knol D, et al. Are psychological factors prognostic indicators of outcome in patients with sub-acute neck pain? *Man Ther* 2010;15(1):111-6.

17. Fitzmaurice GM. Applied longitudinal analysis. Hoboken, N.J.: Hoboken, N.J. : Wiley-Interscience 2004:325-371.

For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

Protected by copyright, including for uses related to text and data mining, AI training, and similar technologies.

Erasmushogeschool .

18. Hoogendoorn WE, Bongers PM, de Vet HC, et al. Comparison of two different approaches for the analysis of data from a prospective cohort study: an application to work related risk factors for low back pain. *Occup Environ Med* 2002;59(7):459-65.
19. Rudolfsson T, Djupsjobacka M, Hager C, et al. Effects of neck coordination exercise on sensorimotor function in chronic neck pain: a randomized controlled trial. *J Rehabil Med* 2014;46(9):908-14.
20. Margolis RB, Tait RC, Krause SJ. A rating system for use with patient pain drawings. *Pain* 1986;24(1):57-65.
21. Atroshi I, Gummesson C, Andersson B, et al. The disabilities of the arm, shoulder and hand (DASH) outcome questionnaire: reliability and validity of the Swedish version evaluated in 176 patients. *Acta Orthop Scand* 2000;71(6):613-8.
22. Dworkin RH, Turk DC, Farrar JT, et al. Core outcome measures for chronic pain clinical trials: IMMPACT recommendations. *Pain* 2005;113(1-2):9-19.
23. Dworkin RH, Turk DC, Wyrwich KW, et al. Interpreting the clinical importance of treatment outcomes in chronic pain clinical trials: IMMPACT recommendations. *J Pain* 2008;9(2):105-21.
24. Vernon H. The Neck Disability Index: state-of-the-art, 1991-2008. *J Manipulative Physiol Ther* 2008;31(7):491-502.
25. Bjorklund M, Wiitavaara B, Heiden M. Responsiveness and minimal important change for the ProFitMap-neck questionnaire and the Neck Disability Index in women with neck-shoulder pain. *Qual Life Res* 2017;26(1):161-70.
26. Carroll LJ, Hogg-Johnson S, Cote P, et al. Course and prognostic factors for neck pain in workers: results of the Bone and Joint Decade 2000-2010 Task Force on Neck Pain and Its Associated Disorders. *Spine (Phila Pa 1976)* 2008;33(4 Suppl):S93-100.
27. Bruls VE, Bastiaenen CH, de Bie RA. Prognostic factors of complaints of arm, neck, and/or shoulder: a systematic review of prospective cohort studies. *Pain* 2015;156(5):765-88.
28. Turk DC, Melzack R. Handbook of pain assessment. 3rd ed. ed. New York ; London: Guilford 2011.

For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

Protected by copyright, including for uses related to text and data mining, AI training, and similar technologies. Erasmushogeschool .

29. Svanborg P, Asberg M. A new self-rating scale for depression and anxiety states based on the Comprehensive Psychopathological Rating Scale. *Acta Psychiatr Scand* 1994;89(1):21-8.

30. Cleland JA, Fritz JM, Childs JD. Psychometric properties of the Fear-Avoidance Beliefs Questionnaire and Tampa Scale of Kinesiophobia in patients with neck pain. *Am J Phys Med Rehabil* 2008;87(2):109-17.

31. Vlaeyen JW, Kole-Snijders AM, Rotteveel AM, et al. The role of fear of movement/(re)injury in pain disability. *J Occup Rehabil* 1995;5(4):235-52.

32. Jensen IB, Linton SJ. Coping strategies questionnaire (CSQ): Reliability of the swedish version of the CSQ. *Cogn Behav Ther* 1993;22(3-4):139-45.

33. Bergstrom G, Jensen IB, Bodin L, et al. Reliability and factor structure of the Multidimensional Pain Inventory -Swedish Language Version (MPI-S). *Pain* 1998;75(1):101-10.

34. Hill JC, Lewis M, Sim J, et al. Predictors of poor outcome in patients with neck pain treated by physical therapy. *Clin J Pain* 2007;23(8):683-90.

35. Wolfe F, Smythe HA, Yunus MB, et al. The american college of rheumatology 1990 criteria for the classification of fibromyalgia. *Arthritis & Rheumatism* 1990;33(2):160-72.

36. Ekblom-Bak E, Hellenius ML, Ekblom O, et al. Independent associations of physical activity and cardiovascular fitness with cardiovascular risk in adults. *Eur J Cardiovasc Prev Rehabil* 2010;17(2):175-80.

37. Leijon O, Wiktorin C, Harenstam A, et al. Validity of a self-administered questionnaire for assessing physical work loads in a general population. *J Occup Environ Med* 2002;44(8):724-35.

38. Vittinghoff E, Glidden DV, Shiboski SC, et al. Regression Methods in Biostatistics, Linear, Logistic, Survival, and Repeated Measures Models. 2nd ed. New York, USA: Springer New York 2012:261-308, 395-429.

39. Hosmer DW, Lemeshow S. Applied logistic regression. 2nd ed. New York ; Chichester: Wiley 2000:91-142, 163.

For peer review only

Protected by copyright, including for uses related to text and data mining, AI training, and similar technologies.

Erasmushogeschool .

40. Steyerberg EW, Borsboom GJ, van Houwelingen HC, et al. Validation and updating of predictive logistic regression models: a study on sample size and shrinkage. *Stat Med* 2004;23(16):2567-86.

41. Schellingerhout JM, Heymans MW, Verhagen AP, et al. Prognosis of patients with nonspecific neck pain: development and external validation of a prediction rule for persistence of complaints. *Spine (Phila Pa 1976)* 2010;35(17):E827-35.

42. Kjellman G, Skargren E, Oberg B. Prognostic factors for perceived pain and function at one-year follow-up in primary care patients with neck pain. *Disabil Rehabil* 2002;24(7):364-70.

43. Verhagen AP, Karels CH, Schellingerhout JM, et al. Pain severity and catastrophising modify treatment success in neck pain patients in primary care. *Man Ther* 2010;15(3):267-72.

44. Beneciuk JM, Bishop MD, George SZ. Clinical prediction rules for physical therapy interventions: a systematic review. *Phys Ther* 2009;89(2):114-24.

45. Woodhouse A, Pape K, Romundstad PR, et al. Health care contact following a new incident neck or low back pain episode in the general population; the HUNT study. *BMC Health Serv Res* 2016;16:81.

46. Bot SD, van der Waal JM, Terwee CB, et al. Predictors of outcome in neck and shoulder symptoms: a cohort study in general practice. *Spine* 2005;30(16):E459-E70.

47. Bohman T, Alfredsson L, Jensen I, et al. Does a healthy lifestyle behaviour influence the prognosis of low back pain among men and women in a general population? A population-based cohort study. *BMJ Open* 2014;4(12).

48. Svedmark A, Bjorklund M, Hager CK, et al. Impact of Workplace Exposure and Stress on Neck Pain and Disabilities in Women-A Longitudinal Follow-up After a Rehabilitation Intervention. *Ann Work Expo Health* 2018;62(5):591-603.

For peer review only

Protected by copyright, including for uses related to text and data mining, AI training, and similar technologies. Erasmushogeschool .

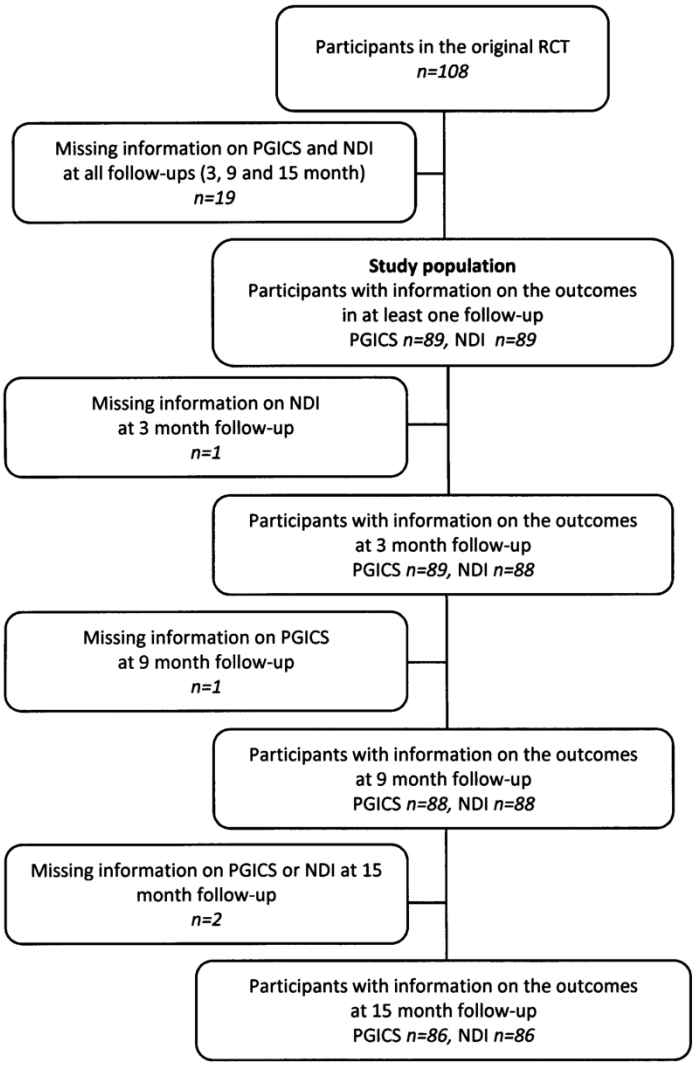

Figure 1. Included participants and progress of participants along the follow-up period concerning the outcome measures. RCT: Randomised controlled trial. PGICS: The Patient Global Impression of Change Scale. NDI: The Neck Disability Index.

206x296mm (300 x 300 DPI)

BMJ Open: first published as 10.1136/bmjopen-2018-024557 on 24 April 2019. Downloaded from http://bmjopen.bmj.com/ on May 15, 2025 at Department GEZ-LTA Erasmushogeschool . Protected by copyright, including for uses related to text and data mining, AI training, and similar technologies.

TRIPOD Checklist: Prediction Model Development

Section/Topic	Item	Checklist Item	Page
Title and abstract			
Title	1	Identify the study as developing and/or validating a multivariable prediction model, the target population, and the outcome to be predicted.	1
Abstract	2	Provide a summary of objectives, study design, setting, participants, sample size, predictors, outcome, statistical analysis, results, and conclusions.	2-3
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.	4-5
	3b	Specify the objectives, including whether the study describes the development or validation of the model or both.	5
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.	5
	4b	Specify the key study dates, including start of accrual; end of accrual; and, if applicable, end of follow-up.	5-6
Participants	5a	Specify key elements of the study setting (e.g., primary care, secondary care, general population) including number and location of centres.	5
	5b	Describe eligibility criteria for participants.	5-6
	5c	Give details of treatments received, if relevant.	NA
Outcome	6a	Clearly define the outcome that is predicted by the prediction model, including how and when assessed.	6-7
	6b	Report any actions to blind assessment of the outcome to be predicted.	NA
Predictors	7a	Clearly define all predictors used in developing or validating the multivariable prediction model, including how and when they were measured.	7-11 Tab 1
	7b	Report any actions to blind assessment of predictors for the outcome and other predictors.	NA
Sample size	8	Explain how the study size was arrived at.	Fig 1
Missing data	9	Describe how missing data were handled (e.g., complete-case analysis, single imputation, multiple imputation) with details of any imputation method.	6, 17-18 Fig 1 Tab 2
Statistical analysis methods	10a	Describe how predictors were handled in the analyses.	11-12 Tab 1, 3 and 4
	10b	Specify type of model, all model-building procedures (including any predictor selection), and method for internal validation.	11-12
	10d	Specify all measures used to assess model performance and, if relevant, to compare multiple models.	12
Risk groups	11	Provide details on how risk groups were created, if done.	NA
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.	Fig 1
	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.	13 Fig 1 Tab 2, 3 and 4
Model development	14a	Specify the number of participants and outcome events in each analysis.	13 Tab 3 and 4
	14b	If done, report the unadjusted association between each candidate predictor and outcome.	Tab 3
Model specification	15a	Present the full prediction model to allow predictions for individuals (i.e., all regression coefficients, and model intercept or baseline survival at a given time point).	Tab 4
	15b	Explain how to the use the prediction model.	18 & 20-21
Model performance	16	Report performance measures (with CIs) for the prediction model.	Tab 4
Discussion			
Limitations	18	Discuss any limitations of the study (such as nonrepresentative sample, few events per predictor, missing data).	20
Interpretation	19b	Give an overall interpretation of the results, considering objectives, limitations, and results from similar studies, and other relevant evidence.	18-20
Implications	20	Discuss the potential clinical use of the model and implications for future research.	21

For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

Protected by copyright, including for uses related to text and data mining, AI training, and similar technologies. Erasmushogeschool .

TRIPOD Checklist: Prediction Model Development

Other information			
Supplementary information	21	Provide information about the availability of supplementary resources, such as study protocol, Web calculator, and data sets.	22
Funding	22	Give the source of funding and the role of the funders for the present study.	22

For peer review only

Protected by copyright, including for uses related to text and data mining, AI training, and similar technologies.
Erasmushogeschool .