

## Research

## Few promising multivariable prognostic models exist for recovery of people with non-specific neck pain in musculoskeletal primary care: a systematic review

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## KEY WORDS

Primary care  
Systematic review  
Neck pain  
Multivariable prognostic models  
Prognosis



## ABSTRACT

**Question:** Which multivariable prognostic model(s) for recovery in people with neck pain can be used in primary care? **Design:** Systematic review of studies evaluating multivariable prognostic models. **Participants:** People with non-specific neck pain presenting at primary care. **Determinants:** Baseline characteristics of the participants. **Outcome measures:** Recovery measured as pain reduction, reduced disability, or perceived recovery at short-term and long-term follow-up. **Results:** Fifty-three publications were included, of which 46 were derivation studies, four were validation studies, and three concerned combined studies. The derivation studies presented 99 multivariate models, all of which were at high risk of bias. Three externally validated models generated usable models in low risk of bias studies. One predicted recovery in non-specific neck pain, while two concerned participants with whiplash-associated disorders (WAD). Discriminative ability of the non-specific neck pain model was area under the curve (AUC) 0.65 (95% CI 0.59 to 0.71). For the first WAD model, discriminative ability was AUC 0.85 (95% CI 0.79 to 0.91). For the second WAD model, specificity was 99% (95% CI 93 to 100) and sensitivity was 44% (95% CI 23 to 65) for prediction of non-recovery, and 86% (95% CI 73 to 94) and 55% (95% CI 41 to 69) for prediction of recovery, respectively. Initial Neck Disability Index scores and age were identified as consistent prognostic factors in these three models. **Conclusion:** Three externally validated models were found to be usable and to have low risk of bias, of which two showed acceptable discriminative properties for predicting recovery in people with neck pain. These three models need further validation and evaluation of their clinical impact before their broad clinical use can be advocated. **Registration:** PROSPERO CRD42016042204. [Wingbermühle RW, van Trijffel E, Nelissen PM, Koes B, Verhagen AP (2018) Few promising multivariable prognostic models exist for recovery of people with non-specific neck pain in musculoskeletal primary care: a systematic review. *Journal of Physiotherapy* 64: 16–23]

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## Introduction

Globally, neck pain is one of the main contributors to years lived with disability.<sup>1,2</sup> Improvements in pain and disability typically occur in the first weeks after the onset of an episode of neck pain, but residual pain and disability beyond this time are often of substantial severity and persist for at least 1 year.<sup>3</sup> High baseline neck pain intensity and disability scores have been identified as predictors for poor outcome in people with neck pain.<sup>4</sup> Cost-effectiveness and short-term beneficial effects of non-invasive primary care treatment have been reported, while long-term effects are still limited.<sup>5–8</sup> Subgrouping of people with neck pain based on their prognosis may enhance treatment outcomes by enabling tailored treatment and management strategies.<sup>9–11</sup> High-quality research on neck pain prognosis has been a research priority for over a decade.<sup>12</sup>

A fundamental shift in clinical practice has been proposed towards the prospective relationships between phenotypic, genomic, and environmental assessment of patients.<sup>13</sup> It is argued that

prognostic profiles allow a more wholistic view and can better manage subjectively reported health problems than diagnostic labels.<sup>13</sup> These prognostic profiles should also more accurately mirror daily practice.<sup>14</sup>

Prognostic factors can be developed based on demographic factors, disease characteristics, or factors derived from history taking, physical examination, or additional examinations (such as imaging, blood assays, urine tests or other biological measurements).<sup>15</sup> Multiple factors are likely to interact with each other, so multivariable prognostic models that consider correlations between predictors have been proposed.<sup>4,16–18</sup> Development of multivariable prognostic models consists of three consecutive stages: developing the model (derivation); validating its performance in new patients (external validation); and studying its clinical impact (impact analysis).<sup>17,19</sup>

Numerous multivariable prognostic models in musculoskeletal primary care for people with neck pain have been developed. To our knowledge, these models have not been evaluated systematically using tools specifically designed to assess quality and

usability of primary multivariable prognostic model studies included in a systematic review.

Several systematic reviews have been conducted to summarise the value of prognostic models in the musculoskeletal domain,<sup>20–22</sup> with one focusing on neck pain alone.<sup>23</sup> These reviews concluded that the methodological quality of the included studies was often poor to moderate, validation studies are rare, and routine clinical use is therefore not supported. Methodological quality was assessed in these systematic reviews using tools not specifically designed for assessing the quality of prediction models. Only recently, PROBAST (Prediction model study Risk Of Bias Assessment Tool) has become available; it is designed to assess the risk of bias and concerns about applicability of studies that develop and/or validate a multivariable prediction model when they are included in systematic reviews.<sup>24–26</sup>

To our knowledge, no systematic review on multivariable prognostic models for recovery (pain reduction, reduced disability, or perceived recovery) of people of all ages presenting in primary care with neck pain has been conducted using up-to-date methodology. The aim of this systematic review was to summarise the validity and applicability of multivariable prognostic models for recovery in people with neck pain in primary care.

Therefore, the specific research question for this systematic review was:

Which multivariable prognostic model(s) for recovery in people with neck pain can be used in primary care?

## Method

### Identification and selection of studies

MEDLINE, EMBASE, and CINAHL databases were searched to retrieve all relevant studies on multivariable prognostic models for recovery of neck pain from inception up to May 3, 2016. This search was based on a validated strategy adapted for the purpose of this study.<sup>20,27,28</sup> The full search strategy is listed in Appendix 1 on the eAddenda. De-duplication was performed in Mendeley and hand-checked.<sup>29</sup> No language restrictions were imposed. Additional manual searching of reference lists of all included studies was performed.

To be eligible for inclusion, studies had to generate multivariable prognostic models using data from prospective cohort studies and randomised, controlled trials on participants of any age with non-serious specific and non-specific neck pain. Models in all stages of their development were considered. Models were defined as those constructed by multivariable analysis from a combination of at least two predictors associated with a particular outcome, while derived models could contain one remaining variable.<sup>17,30,31,32</sup> All baseline characteristics that are feasible to measure in primary care were considered as potential predictors. Studies were included when the outcome concerned pain reduction, reduced disability, or perceived recovery at any time of follow-up. The inclusion criteria are summarised in [Box 1](#). Studies aimed at (cost-)effectiveness, side effects, or developing a questionnaire were excluded. Studies using clinical procedures involving skin penetration like injection, acupuncture, or dry needling were also excluded.

Two reviewers (RW, PN) independently screened records for possibly relevant studies based on title and abstract. Subsequently, full texts of potentially relevant articles were independently assessed for eligibility. Discrepancies between reviewers were resolved through discussion or by a third reviewer (APV).

### Assessment of characteristics of studies

#### Quality

Quality of the selected studies was assessed using the pre-publication version of PROBAST.<sup>36</sup> PROBAST was developed using a

#### Box 1. Inclusion criteria.

##### Models

- Constructed with multivariable analysis
- Combination of at least two predictors
- Any stage of development

##### Design

- Prospective cohort studies
- Randomised, controlled trials

##### Participants

- People of any age
- Non-serious specific or non-specific neck pain at any stage<sup>a</sup>

##### Determinants

- Baseline characteristics at intake
- Applicable to and easily obtained in non-invasive musculoskeletal primary care

##### Outcome to be predicted

- Pain
- Disability
- Perceived recovery

<sup>a</sup> Neck pain was defined as pain located in the anatomic region of the neck from the linea nuchea superior to the spina scapula, with or without radiation to the trunk or upper limb.<sup>33,34</sup> Non-specific neck pain was defined as neck pain without an identified pathological basis. Non-serious neck pain was defined as neck pain with an identified pathological basis, but with no contra-indication for musculoskeletal primary care.<sup>35</sup>

Delphi process involving 40 experts in the fields of systematic review methodology and prediction research. It was designed to assess risk of bias, applicability, and usability of multivariable prediction model studies included in a systematic review using a similar domain-based approach as the revised tool for the quality assessment of diagnostic accuracy studies (QUADAS-2). Judgements on high, low, or unclear risk of bias for reported estimates of the model's predictive performance were made for five key domains (participant selection, predictors, outcome, sample size and participant flow, and analysis) after judgement of signalling questions. As the signalling question was to determine whether there was a reasonable number of outcome events in a logistic regression, the number of events in the smallest group was divided by the total degrees of freedom used during the whole modelling process. Counting degrees of freedom was based on each time a variable or its category was tested on the outcome. Univariable predictors were considered here as part of the whole modelling process if they were selected based on their *p*-value. Rating was according to the 'rule of thumb' of 10 events per variable.<sup>37</sup> For linear regression, the number of participants was divided by the number of predictors. High, low, or unclear concerns about applicability regarding the review question were made in a similar structure for three key domains (participant selection, predictors, and outcome). An overall judgement about risk of bias and applicability of the prediction model evaluation was reached based on a separate summative rating across all domains for derivation and validation studies according to the PROBAST criteria. Finally, a model's usability was rated for its presentation with sufficient detail to be used in the intended context and target population.

Two reviewers (RW, PN) independently assessed the quality of the selected studies. Discrepancies and unclear items were resolved through discussion or, if necessary, adjudication by a third reviewer (APV). Percentage agreement and Cohen's kappa in a 2x2 contingency table were used to describe the level of agreement between the two reviewers for the judgements of the risk of bias and applicability domains. For this purpose, 'high' and 'unclear' ratings were collapsed into one category. Rating of models within the same study were combined into one variable per reviewer, if ratings were the same.

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