Systematic Review

Predictors of Persistent Neuropathic Pain – A Systematic Review

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Background: Characterization of the prognostic variables for persistent neuropathic pain (PNP) remains incomplete despite multiple articles addressing this topic. To provide more insight into the recovery and prognosis of neuropathic pain, high-quality data are required that provide information about the predictors that contribute to the development of PNP.

Objective: To determine the methodological quality of studies about predictors for PNP and to summarize findings of predictors found in high-quality studies.

Study Design: A systematic review.

Setting: VU University Medical Center, Amsterdam, The Netherlands.

Methods: Studies were identified by searching the electronic databases PubMed, Embase, and Cochrane Library. Methodological quality of each article was independently assessed by 2 reviewers.

Results: Forty-six relevant studies were identified, classified into 4 different neuropathic pain (NP)-syndromes: postherpetic neuralgia (n = 35), radicular pain and sciatica (n = 3), postsurgical pain (n = 6), and other types of NP (n = 2). Seven studies were of high quality. The 3 high-quality studies found for PHN reported male gender, older age, smoking, trauma at the site of lesion, missed antiviral prescriptions, higher acute pain severity, higher rash severity, more neuropathic characteristics, shorter rash duration, and a lower health status as predictors for PNP. For persistence of radicular pain one high-quality study reported negative outcome expectancies, pain-related fear of movement, and passive pain coping as predictors for PNP. Psychological distress, acute pain, breast cancer surgery, higher body mass index, area of secondary hyperalgesia, neuropathic characteristics, hypoesthesia, and hyperesthesia were found to be predictive for postsurgical pain in 3 high-quality studies.

Limitations: Some publications may have been missed during literature search. The low-quality of the studies could be the result of an incomplete description of their methods.

Conclusions: High-quality studies mainly assessed factors related to disease functions and structures. Due to shortcomings in methodological quality and limited areas of predictor selection, there is a need for high-quality studies focusing on predictor measurement, statistical analysis and the use of a standardized set of predictors.

Key words: Neuropathic pain, persistent pain, systematic review, literature search, predictors, quality assessment, ICF-model

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Persistence of neuropathic pain (NP) constitutes a considerable problem in current medical practice. NP, which is defined as pain arising as a direct consequence of a lesion or disease affecting the somatosensory system (1), is characterized by spontaneous pain with abnormal sensory symptoms (2-4). Both stimulus-evoked pain, which includes hyperalgesia and allodynia to mechanical or thermal

stimulation, and stimulus-independent pain, such as spontaneous pain described as shooting, lancinating, or burning (2,3,5), can occur. In 6 – 8% of the general population acute NP leads to persistent neuropathic pain (PNP) (6), impairing health-related quality of life and physical and mental health of patients (6,7). Different NP syndromes underlie PNP, such as post-herpetic neuralgia (PHN), diabetic neuropathy, spinal cord injury, and post-traumatic neuralgia (2,4,6,8), but also precipitating factors, such as alcohol dependence, drug abuse, and the activity of chemokines, have been described in this context (9). Appropriate treatments targeting modifiable factors in high-risk patients could help prevent its persistence. However, knowledge about (modifiable) factors that contribute to the persistence of NP is lacking, which makes NP-treatment a challenge for health care (10).

To provide more insight into the recovery and prognosis of NP, high-quality data that provide information about the predictors that contribute to the development of PNP, is required. Information about predictors for PNP is available for several NP-disorders, such as PHN and post-thoracotomy pain. Earlier, by means of a Delphi-survey, we asked experts in the field of NP to give their opinion about potential predictors for PNP in general. Mainly psychological factors and factors related to sensory disturbances were considered important (11). Also, recently, we provided a general overview of predictors for development of PNP described in the literature (12). Without applying any quality weighting, the most common predictors for the development of PNP were older age, psychological factors, higher pain intensity, and sensory signs and symptoms. However, a quality-based appraisal of studies reporting predictors for PNP has not been performed yet. Therefore, we performed this systematic review of the literature with the aim of determining the methodological quality of the studies on predictors for PNP and summarizing findings on predictors found in high-quality studies.

Methods

Search Strategy

Studies were identified by searching the electronic databases PubMed, Embase, and Cochrane Library. Searches were restricted to English, French, German, and Dutch languages. Searches were conducted from the inception date of the databases to November 2014. The following search terms were used to search all databases: chroni*; persist*; neuropath*; neuralgi*; pain; prognos*; and predict*. For PubMed the following terms were added: epidemiologic studies; prevalence; incidence; risk; causality; and etiology. For full electronic search strategies, see Supplementary Table 1. One reviewer (SB) scanned the titles and abstracts and identified potentially relevant articles to be retrieved. Full-text copies were obtained where there was uncertainty. Reference lists of retrieved articles were screened for additional articles.

Inclusion and Exclusion Criteria

Studies were selected when the aim of the study was to determine predictors for persistence of pain in patients with NP syndromes aged 18 years or older. We searched for all possible predictors associated with persistence of pain. Studies were excluded when the complaint of patients under study was not exclusively specified as neuropathic, and when only the efficacy of drugs was investigated as possible predictor of PNP. Also studies about phantom limb pain were excluded. Furthermore, animal studies, reviews, and case reports were excluded. Persistence of NP was accepted in case the outcome of the study was pain. Since there is inconsistency about the definition of persistent pain, we did not define a cut-off point for the start of persistent pain in advance. Also we did not discriminate between definitions and diagnostic tools used to define (neuropathic) pain.

Quality Assessment

Methodological quality evaluation was performed by 3 reviewers (SB, MP, MH), whereby each article was independently assessed by 2 reviewers following the criteria of the "Quality Assessment of Reports of Prognostic Studies" form, described by Veerbeek et al (13). This checklist consists of 27 items investigating 6 major risks of bias: study design, study attrition, predictor measurement, outcome measurement, statistical analysis, and clinical performance/validity. For the complete checklist including explanations for scoring individual items, see Supplementary Table 2. Each item was graded positive, negative, or partial/unknown. Per domain, a low risk of bias was arbitrarily considered when ≥ 75% of the items within the domain were scored positive (13). The total score was the sum of all items graded as positive, with a maximum of 27 points. To determine the influence of the methodological quality of the studies on the reported predictors, predictors out of studies with a total score of ≥ 20 points (75% of the maximum score), were compared to predictors out of studies with a total score of ≥ 13 points (50% of the maximum score). For

the purpose of this study which focused on high-quality articles, information about low-quality studies is provided in Supplementary Table 3. Reviewers performing the assessments were not blinded to author names, institutions, or journal of publication. Discrepancies in quality ratings between reviewers were resolved during a consensus meeting. All percentages were rounded to the nearest whole number.

Data Extraction

One reviewer (SB) extracted the following data from the included studies: study population, gender and age, study design, NP disease, definition of (persistent) NP, duration of follow-up, and statistical analysis used. Effect sizes as odds ratios (OR), hazard ratios (HR), relative risks (RR) and prevalence ratios (PR), 95% confidence interval, and measurement tool of reported predictors were also extracted when available. In some cases the effect size was not available, but sufficient other data existed (Beta, standard error) to calculate the effect size and associated confidence intervals. A factor was considered to be a predictor where there was a significant effect or where the authors described this as such. A factor was considered to be a non-predictor where the effect was not significant.

In the results section, the extracted predictors will be described according to the different follow-up periods where these were provided in the articles. To categorize predictors in different levels of human functioning, we used the International Classification of Functioning, Disability and Health (ICF) model as a framework (14,15).

Results

Study Inclusion

In total, 2,434 eligible articles were found. Searching the reference lists of these articles, an additional 162 articles were retrieved. There were 2,459 articles excluded because the article was a review, the study population was not specified as NP patients, the articles did not assess predictive factors, or the article was in a language other than English, French, German, or Dutch. The full texts of the remaining 137 studies were examined. Finally, 46 studies met the inclusion criteria and were included in this systematic review, comprising 7 randomized controlled trials (RCTs), 32 prospective studies, 4 retrospective studies, and 3 cross-sectional studies. The other 91 articles were excluded because the study population was not specified as NP patients, the article did not assess predictive factors for PNP, the study was performed with children, or because the article was a review. For details of article selection, see Fig. 1.

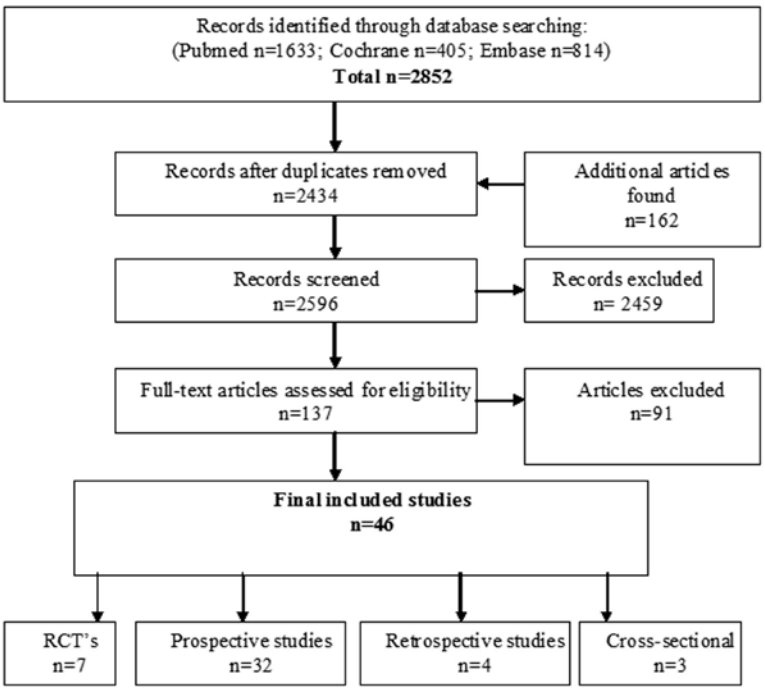

Fig.1. Flow diagram of included studies.

Study Characteristics

The number of participants included in the 46 identified studies ranged from 19 (16) to 3,312 (17), with a total of 19,394 participants. The identified articles can be classified into 4 different NP-syndromes: PHN (35 studies), radicular pain and sciatica (3 studies), postsurgical pain (post-thoracotomy pain, persistent postsurgical pain, and post-mastectomy pain syndrome) (6 studies), and other types of NP (2 studies about PNP after oxaliplatin neurotoxicity and complex regional pain syndrome). Eight studies provided a specified definition of NP (17-24).

The definition of PNP and follow-up duration varied between studies. In 7 studies a specific pain intensity (with a validated pain scale) (19,21,25-29) was used to define PNP, whereas other studies used a specific pain duration. The follow-up duration between studies ranged from one month (19,30-34) to 9 years (35); a follow-up duration of 3 months was most frequently used (16,22,24-26,28,29,32,36-42). In 3 studies the duration of follow-up was not specified (17,43,44).

Quality Assessment

Table 1 shows the quality scores on each item as well as the total scores of each study. As none of the articles addressed the quality criterion "external validation," this criterion was excluded from further analyses. Most studies had a high risk of bias; the median methodological quality score for the evaluated studies was 14 points (SD 4.3), with a range of 6 to 22 points. Seven (15%) of the 46 studies were of high methodological quality (score ≥ 20 points) (21,22,29,33,36,45,46).

Study Design

Half of the included studies properly described the sampling frame and recruitment procedure. Both inclusion and exclusion criteria were reported by 45% of the studies. The baseline characteristics of gender, age, and pre-existing pain were described in 72% of the studies. In 80% a prospective design was used. Of the included studies, 39% received a positive score on ≥ 75% of the items in the domain "study design."

Study Attrition

In 67% of the included studies the number of patients lost to follow-up was reported and did not exceed 20% of the study population. Reasons for loss to follow-up were reported in 46% of the studies. In case of missing values, 22% used an appropriate method to deal with missing data. Overall, 20% of the included studies received a positive score on ≥ 75% of the items in the domain "study attrition."

Predictor Measurement

Seventy-one percent of the identified studies clearly described all candidate predictors and 59% measured one or more candidate predictors with a valid and reliable method. Only 33% stated cut-off points with rationale for all possible predictors. In total, 41% of the included studies received a positive score on ≥ 75% of the items in the domain "predictor measurement."

Outcome Measurement

A clear definition of the outcome of interest was stated in 94% of the studies. A valid and reliable method for measuring the outcome was used in 57%, as well as the use of a coding scheme and cut-off points. For the domain "outcome measurement," 59% of the articles scored positive on ≥ 75% of the items.

Statistical Analysis

In 44% of the articles the strategy for model building was described. A sufficient sample size was seen in 37% of the included studies. Only in 22% of the articles was the univariable analysis shown, while 50% properly presented the multivariable model with point estimates and confidence intervals. The domain "statistical analysis" received a positive score on ≥ 75% of the items in only 15% of the included studies.

Clinical Performance/internal Validity

Clinical performance was tested in 20% of the identified articles, while only 4% used appropriate techniques to assess internal validity. None of the articles validated the model in a second independent group of patients. None of the studies scored positive on ≥ 75% of the items in this domain.

Predictors for Persistent Neuropathic Pain

The main characteristics (predictors, non-predictors, and effect sizes) of the high-quality studies can be found in Table 2. (For information about low-quality studies see Supplementary Table 3. Not all references in the Supplementary Table 3 are included in the main article. Therefore, see Supplementary Table 3 for additional references of low quality studies).

Predictors for Persistent Neuropathic Pain in High-Quality Studies

Seven high-quality studies were identified

Table 1. *Quality assessment of included studies.*

	Study design						Study attrition				Predictor measurement				Outcome measurement					Statistical analysis					Clinical performance/ validity			
Reference	**D1**	**D2**	**D3**	**D4**	**D5**	**D6**	**A1**	**A2**	**A3**	**A4**	**P1**	**P2**	**P3**	**P4**	**O1**	**O2**	**O3**	**O4**	**O5**	**S1**	**S2**	**S3**	**S4**	**S5**	**C1**	**C2**	**C3**	**Total (/26)**
High quality studies																												
Den Boer 2006	1	1	1	1	1	1	1	1	0	1	1	1	1	?	1	1	1	1	1	1	1	0	1	1	1	?	?	22
Masselin-Dubois 2013	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	?	?	1	1	?	?	?	22
Martinez 2012	1	1	1	1	1	1	1	1	?	0	1	1	1	1	1	1	1	1	1	1	1	?	1	1	?	?	?	21
Bouhassira 2012	1	1	1	1	1	1	1	0	?	?	1	1	1	1	1	1	1	1	1	1	1	1	1	1	?	?	?	21
Opstelten 2007	1	1	1	1	1	1	?	?	1	?	1	1	1	1	1	1	1	1	1	?	0	1	1	1	1	1	?	21
Johansen 2012	1	1	1	0	1	1	1	1	1	1	1	1	?	1	1	1	1	0	1	1	1	1	1	?	?	?	?	20
Parruti 2010	1	?	1	1	1	1	1	1	0	?	1	?	0	1	1	1	1	1	1	1	1	1	1	1	?	1	?	20
Low quality studies																												
Peul 2008	1	1	1	1	?	1	1	1	1	1	?	1	?	1	1	1	?	1	1	1	1	1	1	?	?	?	?	19
Katz 2005	?	1	1	0	1	0	1	0	?	1	1	1	1	1	1	1	1	0	1	1	0	?	1	1	1	?	?	17
Beutner 1995	?	1	1	1	1	1	1	1	1	?	?	1	?	1	1	1	1	1	1	?	1	?	1	0	?	?	?	17
Drolet 2010	1	?	1	1	1	1	1	?	0	?	?	1	?	1	1	1	1	1	1	1	?	0	1	0	1	?	?	16
Haythornwaite 2003	1	1	1	1	?	1	0	?	?	?	1	1	1	1	1	1	1	1	1	1	0	0	0	1	?	?	?	16
Haanpaa 2000	?	1	1	1	1	1	0	?	?	?	1	1	?	1	1	1	1	1	1	?	1	0	1	0	1	?	?	16
Opstelten 2002	1	?	?	?	?	1	1	1	1	1	1	1	1	1	1	0	1	0	1	1	1	0	1	0	?	?	?	16
Coen 2006	1	1	?	1	1	1	1	?	?	?	1	1	?	?	1	1	?	1	1	?	1	1	1	0	1	?	?	16
Petersen 2010	?	1	1	1	?	1	1	?	?	?	1	1	0	1	1	1	1	1	1	1	0	?	1	?	?	?	?	15
Kurokawa 2002	1	1	1	1	1	1	1	1	1	1	0	?	0	1	1	?	1	1	1	?	0	0	?	?	?	?	?	15
Harding 1987	1	1	1	1	1	?	1	1	?	?	1	1	1	1	1	?	1	?	1	?	0	?	?	1	?	?	?	15
Decroix 2000	?	1	1	1	1	1	1	1	?	?	?	?	1	1	1	?	1	1	?	?	1	?	1	1	?	?	?	15
Nurmikko 1990	?	?	1	1	0	1	1	1	1	1	?	1	1	?	1	?	?	1	1	1	0	0	1	1	?	?	?	15
Wilson 2013	1	?	1	0	0	1	?	?	?	?	1	?	1	1	1	0	1	0	1	1	1	1	1	1	?	?	?	13
Jung 2004	1	1	?	1	1	1	1	?	0	1	1	?	?	?	1	?	?	1	?	1	1	0	1	0	1	?	?	14
Haanpaa 1999	?	?	1	1	?	?	1	1	?	?	1	1	1	1	1	1	1	1	1	?	0	0	1	0	?	?	?	14
Dworking 1992	?	?	1	1	1	?	1	?	?	?	1	1	1	?	1	1	?	1	1	1	0	1	0	1	?	?	?	14
Leplow 1990	1	0	1	0	?	1	1	1	0	0	1	1	?	0	1	1	1	?	1	?	0	1	?	?	1	?	?	13
Attal 2009	0	1	1	?	1	1	0	?	?	?	1	1	0	1	1	1	1	1	1	?	0	?	?	0	?	?	?	12
Fabro 2012	1	1	?	1	1	0	1	1	0	0	?	0	1	1	1	1	?	1	0	1	?	0	?	?	?	?	?	12
Thyregod 2007	0	1	1	1	0	1	1	1	?	0	0	0	0	1	1	1	1	1	1	0	?	0	0	0	0	0	0	12
Whitley 1999	?	?	1	1	1	1	?	?	?	?	1	?	0	1	1	?	1	1	?	1	1	?	1	0	?	?	?	12
Quinlivan 2007	1	?	1	1	1	0	0	?	?	?	1	1	?	1	1	?	?	1	1	1	?	0	?	?	?	?	?	11
Zaal 2000	1	1	1	1	1	1	1	?	?	?	1	0	?	1	0	?	?	1	1	?	?	0	?	?	?	?	?	11

Table 1 (cont.). *Quality assessment of included studies.*

	Study design						Study attrition				Predictor measurement				Outcome measurement					Statistical analysis					Clinical performance/ validity			
Reference	**D1**	**D2**	**D3**	**D4**	**D5**	**D6**	**A1**	**A2**	**A3**	**A4**	**P1**	**P2**	**P3**	**P4**	**O1**	**O2**	**O3**	**O4**	**O5**	**S1**	**S2**	**S3**	**S4**	**S5**	**C1**	**C2**	**C3**	**Total (/26)**
Baron 1997	?	1	1	1	0	1	?	?	?	?	1	1	?	1	1	1	?	1	1	?	?	0	?	?	?	?	?	11
Nagasako 2002	?	?	1	1	1	1	?	?	?	?	1	?	?	1	1	1	1	1	0	0	1	?	0	0	?	?	?	11
Choo 1997	1	?	?	0	?	1	1	1	1	1	?	?	?	1	1	0	1	0	1	?	0	?	1	0	?	?	?	11
Meister 1998	?	?	?	1	?	1	?	?	?	?	1	?	?	?	1	?	1	1	1	1	1	?	?	?	1	?	?	10
Duale 2011	0	?	1	1	1	1	1	0	?	?	1	1	0	?	1	?	0	0	1	?	?	0	?	0	?	?	?	9
Quinlivan 2011	1	?	?	1	?	0	1	?	?	?	?	1	0	0	?	0	0	1	1	1	0	?	1	1	?	?	?	9
Searle 2009	1	?	?	1	?	1	0	1	?	?	?	1	?	?	1	1	?	1	1	?	?	0	?	?	?	?	?	9
Gehling 2003	1	?	1	0	?	1	1	?	0	0	1	0	?	1	1	0	0	?	1	?	?	1	?	?	?	?	?	9
Zak-Perlich 2003	1	?	?	1	1	1	?	?	?	?	1	1	?	1	1	?	?	0	1	0	0	0	0	0	?	?	?	9
Miranda 2002	1	?	1	1	1	?	0	?	?	?	1	0	?	0	1	1	?	1	1	?	?	?	?	?	?	?	?	9
Goh 1997	1	?	1	0	?	1	1	?	1	?	1	?	?	1	1	?	?	?	1	?	?	?	?	?	?	?	?	9
Bruxelle 1995	?	1	?	1	1	1	1	1	?	?	?	?	?	1	?	?	?	1	?	?	1	?	?	?	?	?	?	9
Scott 2003	?	?	?	1	1	1	0	?	?	?	1	?	?	?	1	1	?	1	1	?	?	?	?	?	?	?	?	8
Riopelle 1984	?	?	?	1	1	1	1	1	?	?	1	?	?	?	1	?	?	0	1	?	0	0	0	0	?	?	?	8
McKendrick 2009	1	?	?	1	?	1	0	1	?	?	?	?	?	?	1	?	?	?	1	?	?	0	?	?	?	?	?	6
% positive	60.9	50.0	71.7	80.4	63	82.6	67.4	45.7	21.7	21.7	71.7	58.7	32.6	69.6	93.5	56.5	56.5	71.7	87	43.5	37.0	21.7	50.0	30.4	19.6	4.3	0	
≥75% positive per domain	39.1%						19.6%				41.3%				58.7%					15.2%					0%			

D Study design; A Study attrition; P Predictor measurement; O Outcome measurement; S Statistical analysis; C Clinical performance/validity. D1 Source population and recruitment; D2 Inclusion and exclusion criteria; D3 Important baseline key characteristics of study sample; D4 Prospective design; D5 Inception cohort; D6 Information about treatment; A1 Number of loss to follow-up; A2 reasons for loss to follow-up; A3 Methods dealing with missing data; A4 Comparison completers and non-completers; P1 Definition of predictors; P2 Measurement of predictors reliable and valid; P3 Coding scheme and cut-off points; P4 Data presentation; O1 Outcome(s) defined; O2 Measurement of predictors reliable and valid; O3 Coding scheme and cut-off points described; O4 Appropriate end-points of observation; O5 Data presentation; S1 Strategy for model building described; S2 Sufficient sample size; S3 Presentation univariable analysis; S4 Presentation multivariable analysis; S5 Continuous predictors; C1 Clinical performance; C2 Internal validity; C3 External validity. 1 positive; 0 negative; ? partial/unknown. ≥75% positive per domain: percentage of studies in which ≥75% of the items within a domain were scored positive.

Table 2. *Characteristics and predictors for persistence of neuropathic pain of high-quality studies.*

Art	Qas	Patient group	Study design	Definition PNP + follow-up	Statistical analysis	Predictors/Non- Predictors	Effect	95% CI	Measurement
Postherpetic Neuralgia (PHN)									
Bouhassira et al 2012 (36)	21	N = 1354; mean age 67.7 yrs; 62.2% female	COH P	Persistent zoster-related pain at 3 months	Backward logistic regression model	**Predictors**			
						Male gender	OR 1.81	1.11 - 2.94	
						Older age	OR 1.28	1.05 - 1.55	
						More neuropathic characteristics	OR 1.78	1.03 - 3.06	DN4
						Higher pain severity	OR 1.18	1.05 - 1.31	ZBPI
						Lower health status	OR 0.72	0.55 - 0.92	PCS
						Non- Predictors			
						Higher intensity of NP-characteristics	-	-	NPSI
						Higher intensity of brush-evoked allodynia	-	-	
						Lower MCS scores	-	-	MCS
Opstelten et al 2007 (29)	21	N = 598; mean age 66.2 yrs; 60.9% female	RCT	Zoster-associated pain (VAS ≥ 30), 3 months	Backward multivariable logistic regression analysis	**Predictors**			
						Older age	OR 1.08	1.04-1.12	Increase per year
						Higher acute pain severity	OR 1.02	1.01-1.03	VAS
						Higher rash severity	OR 2.31	1.16-4.58	Mild/moderate/severe
						Shorter rash duration	OR 0.78	0.64-0.97	In days
						Non- Predictors			
						Female gender	OR 0.907	0.492-1.671	
						Duration of prodromal pain	OR 0.925	0.834-1.024	
						Antiviral medication	OR 1.821	0.923-3.595	
						Negative self-efficacy	OR 0.999	0.986-1.013	Pain cognition list
						Pain catastrophizing	OR 0.999	0.986-1.012	Pain cognition list
						Positive expectations	OR 1.003	0.992-1.015	Pain cognition list
						Resignation	OR 0.999	0.988-1.009	Pain cognition list
						Trust in health care	OR 1.015	1.002-1.028	Pain cognition list
						State anxiety	OR 0.994	0.963-1.025	STAI
						Trait anxiety	OR 0.984	0.954-1.014	STAI
Parruti et al 2010 (33)	20	N = 441; mean age 58.1 yrs, 43.5% males	COH P	Pain at 1 month and 3 months	Forward logistic regression	**Predictors**			
						Older age (10 year increase)	OR 1.01 (1m)	1.00-1.02	
						Trauma at the site of lesion 6 months before enrollment	OR 2.22 (1m) / OR 2.53 (3m)	1.12-4.39 (1m) / 1.37-4.65 (3m)	
						Missed antiviral prescription	OR 2.01 (1m) / OR 2.28 (3m)	1.01-4.46 (1m) / 1.04-4.98 (3m)	
						Current/former smoker (3m)	OR 2.08 (3m)	1.22-3.55	
						Intense pain at presentation	OR 2.41 (1m) / OR 2.19 (3m)	1.43-4.04 (1m) / 1.32-3.65 (3m)	VAS 100 mm
						Non- Predictors			
						Older age (10 year increase)	OR 1.01 (3m)	0.99-1.02	
						Female gender	OR 1.05 (1m) / OR 1.39 (3m)	0.68-1.63 (1m) / 0.84-2.30 (3m)	
						Current/former smoker (1m)	OR 1.62 (1m)	0.98-2.67	
						Surgical intervention	OR 1.60 (1m) / OR 1.33 (3m)	0.98-2.63 (1m) / 0.79-2.25 (3m)	

Table 2 (cont.). *Characteristics and predictors for persistence of neuropathic pain of high-quality studies.*

Art	Qas	Patient group	Study design	Definition PNP + follow-up	Statistical analysis	Predictors/Non- Predictors	Effect	95% CI	Measurement
Radicular pain & sciatica									
Den Boer et al 2006 (45)	22	N = 277; mean age 43 yrs; 50% female	COH P	Greater pain intensity at 6 weeks and 6 months after surgery for lumbosacral radicular syndrome	Multiple regression analysis	**Predictors** Negative outcome expectancies	OR 1.47*	1.19 - 1.83	4-point Likert scale
						Non- Predictors Pain-related fear of movement Passive pain coping	OR 1.04** OR 1.04***	0.98 - 1.10 0.92 - 1.17	TSK-AV PCI
Postsurgical Pain									
Masselin-Dubois et al 2003 {2013?} (22)	22	N = 59; total knee arthroplasty group: mean age 69.4 yrs, 69.6% female; breast surgery group: mean age 61.4 yrs, 100% female	COH P	Presence of pain with a neuropathic component (based on a score of ≥ 3/7 on the DN4 questionnaire) at 3 months after knee or breast surgery	Multiple logistic regression, backward	**Predictors** Pain at 2 days Breast cancer surgery	OR 3.82 OR 7.83	1.3 - 17.4 1.8 - 28.5	BPI
						Non- Predictors Psychological variables	-	-	
Martinez et al 2012 (46)	21	N = 82; mean age 49.8 yrs; 44% female	COH P	PPSP: pain with neuropathic characteristics (positive DN4 test) at 3 months after iliac crest bone harvest	Logistic regression analysis	**Predictors** Area of secondary hyperalgesia at 48hrs Neuropathic characteristics (positive DN4 test)	OR 1.02 OR 1.75	1.0 - 1.04 1.1 - 2.6	Von Frey Monofilament DN4
						Non- Predictors Presence of hypoesthesia at 48hrs Intensity of pain at 48 hrs	OR 2.06 OR 1.2	0.34 - 12.2 0.9 - 1.5	Von Frey Monofilament NRS
Johansen et al 2012 (21)	20	N = 2043; mean age 57 yrs; 52.1% female	Cross-sectional	PPSP: surgery 3-36 months before survey and NRS ≥ 1	Multiple logistic regression, backward	**Predictors** Psychological distress Hypoesthesia Hyperesthesia Higher Body Mass Index	OR 1.69 OR 2.68 OR 6.27 OR 1.02	1.22-2.36 1.05-3.50 4.43-8.86 1.00-1.05	Hopkins Symptom Checklist
						Non- Predictors Older age Female gender Hypertension Diabetes Time from surgery	OR 0.93 OR 1.02 OR 0.98 OR 0.73 OR 0.94	0.86-0.99 0.86-1.22 0.82-1.17 0.49-1.08 0.90-0.99	

Articles ordered according to their methodological quality score.
Art: article; Qas: Quality assessment (/27). OR: Odds ratio. RCT: Randomized Controlled Trial; COH P: prospective cohort. VAS: Visual Analogue Scale; ZBPI: Zoster Brief Pain Inventory; PCS: Physical Component Summary; NPSI: Neuropathic Pain Symptom Inventory; MCS: Mental Component Summary; STAI: Spielberger's State-Trait Anxiety Inventory; TSK-AV: Tampa Scale of Kinesiophobia; PCI: Pain Coping Inventory; PPSP: Persistent Postsurgical Pain; BPI: Brief Pain Inventory; DN4: Douleur neuropathique 4 questionnaire. Own calculations based on: *B (Beta) 0.39, (SE) standardized error 0.11; **B 0.04, SE 0.03; ***B 0.04, SE 0.06.

(21,22,29,33,36,45,46). Three of them, Bouhassira et al (36), Opstelten et al (29), and Parruti et al (33), described predictors for PHN at 3 (29,36) months follow-up and one and 3 (33) months follow-up. They found older age, male gender, current or former smoker, trauma at the site of lesion 6 months before enrollment (defined as any type of trauma at the site of lesions, such as contusions, burnings, wounds, poly-traumas involving the reactivation site, recalled by the patient), more neuropathic characteristics (a positive Douleur Neuropathique 4 questionnaire (DN4) test), missed antiviral prescription, lower health status, higher acute pain severity, and shorter rash duration to be predictive. These predictors can be divided over the categories personal factors, environmental factors, functions and structures, and health-related quality of life of the ICF-model. Older age and a higher acute pain severity were found to be predictors in all 3 studies.

One identified high-quality study was found for lumbosacral radicular syndrome (45), which described negative outcome expectancies, pain-related fear of movement, and passive pain coping as predictors for PNP after 6 months. All these predictors fell in the psychological category and can therefore be classified as personal factors.

Three high-quality studies were found in the area of postsurgical pain (21,22,46). Masselin-Dubois et al (22) reported pain at 2 days (defined as pain higher than 3 on the Visual Analogue Scale [VAS]) and breast surgery compared to knee surgery as predictors for PNP. In the study of Martinez et al (46), the area of secondary hyperalgesia at 48 hours and neuropathic characteristics were revealed to be predictive factors. Johansen et al (21) found psychological distress and a higher body mass index, hypoesthesia, and hyperesthesia to be predictive for persistent postsurgical pain. Nearly all predictors for postsurgical NP fall in the ICF-domain functions and structure. Only psychological distress is a personal factor.

In total, 34 possible predictors were evaluated, of which 18 were found to be a significant predictor in the ICF-domains personal factors (7), environmental factors (2), functions and structure (8), and participation and health-related quality of life (1). Only higher acute pain severity was frequently reported as a predictor (in 4 out of 7 studies) and female gender was frequently found to be a non-predictor (evaluated in 4 out of 7 studies). However, the evaluated predictors show small effect sizes.

Comparison of Predictors and Non-Predictors Between High- and Low-Quality Studies

In total, 140 possible predictors were measured in 39 low-quality studies. Of these, 53 were found to be a significant predictor. For PHN, most predictors were found in the ICF-categories personal factors and functions and structure, with mainly PHN-specific factors in the last category. The emphasis of other NP-syndromes is directed more towards psychological factors (ICF-category personal factors).

Due to the small number of high-quality studies (n = 7; 15%) evaluated in this review, the large diversity of predictors, and the fact that most predictors were only evaluated in one study, no clear comparison can be made between low- and high-quality studies. However, based on absolute numbers of evaluated predictors, the predictors chosen to be evaluated in high-quality studies were predominantly in the domain of personal factors, whereas in low-quality studies the focus was mainly directed towards functions and structures. In both high- and low-quality studies the categories activities, participation, and health related quality of life received less attention.

For both high- and low-quality studies, older age was consistently found in most studies to be a predictor for PNP (in 2 out of 3 high-quality studies and in 20 out of 29 low-quality studies). Also higher acute pain severity was frequently assessed and found to be a predictor in 2 high-quality studies and in 15 out of 20 low-quality studies.

The Influence of Methodological Quality

The results described above were based on studies that reached the level of 75% of the maximum quality score. To determine whether methodological quality would influence the number and type of predictors, we also evaluated the outcome (number and type of predictors) using a lower cut-off point for methodological quality (50% of the maximum quality score). In this case, 18 additional studies could be added as high-quality (16,23,25-28,32,37-39,41,44,47-52), which resulted in a total of 25 high-quality studies (Supplementary Table 3) wherein 130 different predictors were considered, of which 48 were reported to be statistically significant. Most of these predictors fell in the ICF-domain functions and structure (23), followed by personal factors (17), environmental factors (5), and participation and health-related quality of life (3). When these predictors were compared to the already described predictors in

Table 1, the areas of the ICF where predictors were found remain equal, although the focus moved to functions and structure. However, the evidence of older age and acute pain severity to be predictive factors for PNP is strengthened.

Discussion

The aim of the present review was to provide a systematic overview of predictors for PNP. Only 7 included studies were of high quality, which resulted in 10 predictive factors for PHN (older age, male gender, smoking, trauma at the site of lesion 6 months before enrollment, missed antiviral prescriptions, higher acute pain severity, more neuropathic characteristics, higher rash severity, shorter rash duration, and lower health status), 3 predictors for persistence of radicular pain (negative outcome expectancies, pain-related fear of movement, and passive pain coping) and 8 predictors for postsurgical pain (psychological distress, higher body mass index, pain at 2 days (VAS > 3), breast cancer surgery compared to knee surgery, area of secondary hyperalgesia at 28 hours, neuropathic characteristics, hypoesthesia and hyperesthesia). Although these predictors were found to be related with the occurrence of PNP, most of them have shown low effect sizes which limits their use in the prediction of PNP. Furthermore, more high-quality studies for each NP-disorder are warranted to compare predictors across different disorders. Additionally, the small number of high-quality studies identified prohibits generalization of these results to NP in general. The knowledge of predictors for PNP may improve treatment of NP when these predictive factors can be modified and targeted for treatment. Of the predictors found in this review, smoking, higher acute pain intensity, psychological factors, higher body mass index, and health status can be considered modifiable factors.

To answer the question whether methodological quality influences the outcome, we lowered the cut-off score for high-quality to 50% of the maximum quality score which resulted in 18 more high-quality studies. This lower cut-off point resulted in a higher number of predictors in the ICF-domain functions and structure instead of personal factors, and a strengthening of the evidence for older age and a higher acute pain severity as predictive factors for PNP.

Only 7 out of 46 studies were assessed as high-quality. The main methodological limitations in the included articles were related to study attrition, predictor measurement, statistical analysis, and clinical performance. The criterion external validation appeared to be the only item that was not scored positive in any of the studies, which suggests that this criterion is probably inapplicable or at least very difficult to apply in prognostic studies of pain. The outcome measurements were best described and analyzed, although there was a large heterogeneity with regard to the duration of follow-up and follow-up measurement. We found considerable inconsistency with regard to the definition of NP between studies. Furthermore, in 2008 this definition was revised by Treede et al (1), but the few studies included in this review which were published after this period did not incorporate this new definition. For instance, definitions used were "the presence of documented sensory symptoms in the zoster dermatome" (19), "intense leg pain in an area served by 1 or more spinal nerve roots and is occasionally accompanied by neurological deficits" (23), "low back pain radiating below the knee" (17), "a S-LANSS score (Leeds Assessment of Neuropathic Symptoms and Signs) of twelve or more" (24), and "objective sensory loss with distal distribution at the feet or hand associated with mild symptoms of limb" (18). Also, the cut-off point for persistence of NP differs between studies, which makes it difficult to compare the individual predictors. For instance, a factor can be a predictor for PNP after 6 months but not after one month. For example, PHN is usually seen as persistent at 3 months after a rash onset (26,53), but some studies limit their follow-up measurement to 30 days, therefore the classification "persistent" may be questionable in these cases (19). Considering these shortcomings, there is a need for improvement of methodological quality of future prediction studies. A standardized use of the revised definition and an overall improvement of statistical analysis specified to prediction research may improve the quality of these studies in the future.

Regarding the ICF-domains, personal factors and functions and structures were most frequently examined as predictors and non-predictors. However, the personal factors older age, male gender, and smoking were either found to be a predictor in high-quality studies, while female gender found to be a non-predictor in high-quality studies but was frequently considered predictive in low-quality studies. Activity, participation, and quality of life related factors were least frequently investigated. Reasons for the lack of predictors in these categories could be that authors consider these categories more as an outcome of pain rather than a trigger for persistence of pain and the fact that these factors are more difficult to measure. Therefore, more research

has to be performed to evaluate in what extent factors like health-related quality of life, participation, and physical activity can be considered predictors for PNP. Furthermore, lifestyle related factors were also infrequently evaluated. Smoking was reported as predictive factor in only one high-quality study. In low-quality studies, body mass index was researched once but was not found significant, and smoking twice. This suggest that smoking and a higher body mass index may have an influence on the persistence of NP, but more research has to reveal the extent of this influence.

The large number of predictive studies in the field of PHN identified in our review shows the interest of predictive factors in research on this syndrome. However, this large number of studies could be the result of a higher incidence of PHN compared to other NP-disorders (54) or because of the more uniform diagnosis of PHN. The limited amount of studies aiming to find predictors for the development of other NP syndromes indicates that still a lot of work has to be done in this area. A number of prediction studies in the field of persistent pain in general are available, but are not, or are only partly, directed at NP (55-58).

Limitations

This review has several limitations. First, there is a possibility that some publications were missed during the literature search due to poor indexing of predictor studies or publication bias. Second, only one reviewer performed the literature search. Also, several studies show predictive factors for treatment response in patients with different NP syndromes (59-62). However, these studies were also excluded in this review because the studied patients already had persistent pain at the start of the study. Studies about postoperative pain syndromes were included, of which pain could be mixed (both neuropathic and nociceptive). Finally, the quality ratings are based on apparent quality as described in the articles, which means that a study could have used high-quality methods but not described it as such in the publication. Furthermore, the fact that we excluded the quality criterion external validation from the quality list does not mean that this criterion is not important in prediction research. In fact, external validation should ideally be conducted to determine the generalizability of the prognostic model. The checklist used to determine the quality of the studies also needs a critical note. The development of a valid and reliable checklist for prognostic studies is still in progress. The checklist of Veerbeek et al (13) is suitable for prognostic studies and therefore used in the present review. However, their checklist was based on prior systematic reviews of prognostic studies mainly in patients with stroke and was adopted to be used for prognostic models for pain patients.

Conclusion

A large number of studies have been performed in search of predictors for persistence of NP, although mainly of low-quality and in the area of PHN. High-quality studies are therefore warranted for PHN as well as for other NP-disorders. Improvement is required with regard to the assessment of predictors, the statistical analysis, and clinical performance. Furthermore, the revised definition of NP should be used consistently. The results show that predictors and non-predictors are now mainly focused on personal factors and functions and structure, with indications for differences between high- and low-quality studies. Therefore, with the use of a standardized set of predictors in all ICF-domains the predictive value of activities and participation can also be assessed. Although health-related quality of life is frequently used as an outcome factor of NP, this factor may also be related to persistence of NP and therefore should be evaluated in future prediction research.

Acknowledgement

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Supplementary Table I: Search strategies in all databases

Search in PubMed (MEDLINE)
(chroni*[tiab] OR persist*[tiab] OR (chronic disease[mesh]))
(neuropath*[tiab])
(neuralgia[mesh] OR neuralgi*[tiab])
(pain*[tiab] OR pain[mesh])
(((((("Epidemiologic Studies"[mesh] OR risk[mesh]) OR prognosis[mesh] OR prognos*[tiab]) OR predict*[tiab]) OR (Prevalence[mesh] OR Epidemiology[mesh] OR epidemiology[subheading])) OR incidence[mesh]) OR (causality[mesh] OR etiology[subheading])
case reports[pt]
review[pt]
((1 AND 2 AND 4) OR (1 AND 3))
8 AND 5
(8 AND 5) NOT (animals[mh] NOT humans[mh]))
10 NOT (6 OR 7)
10 NOT (6 OR 7) Limits: English, French, German, Dutch

Search in Embase
neuralgia/exp
neuralgi*:ab,ti
neuropath*:ab,ti
persist*:ab,ti
chroni*:ab,ti
pain/exp
pain*:ab,ti
prediction and forecasting/exp
predict*:ab,ti
prognosis/exp
prognos*:ab,ti
((((4 OR 5) AND 3) AND (6 OR 7)) OR ((1 OR 2) AND (4 OR 5)))
(12 AND (8 OR 9 OR 10 OR 11))

Search in Cochrane
chroni*:ti,ab,kw
persist*:ti,ab,kw
neuropath*:ti,ab,kw
neuralgi*:ti,ab,kw
pain*:ti,ab,kw
(((1 OR 2) AND 3 AND 5) OR (4 AND (1 OR 2)))

Supplementary Table II: Quality assessment of reports of prognostic studies (1)

OUTCOME STRATEGIES		SCALE	CRITERIA
Study design			
D1	Source population and recruitment	Y/N/?	Positive when sampling frame (e.g. hospital-based, community-based, primary care) and recruitment procedure (place and time-period, method used to identify sample) are reported.
D2	Inclusion and exclusion criteria	Y/?	Positive if both the inclusion and exclusion criteria are explicit described.
D3	Important baseline key characteristics of study sample	Y/?	Positive if the following key characteristics of the sample are described: gender, age, pre-existing pain.
D4	Prospective design	Y/N/?	Positive when a prospective design was used, or in case of a historical cohort in which prognostic factors are measured before the outcome is determined.
D5	Inception cohort	Y/N/?	Positive if observation started at a uniform time point.
D6	Information about treatment	Y/N/?	Positive if information on treatment during observation period is reported (e.g. (para)medical, usual care, randomized, etc.).
Study attrition			
A1	Number of loss to follow-up	Y/N/?	Positive if number of loss to follow-up during period of observation did not exceed 20%.
A2	Reasons for loss to follow-up	Y/N/?	Positive if reasons for loss to follow-up are specified, or there was no loss to follow-up.
A3	Methods dealing with missing data	Y/N/?	Positive, if in case of missing values the method of dealing with missing values is adequate (e.g. multiple imputation), or there are no missing values.
A4	Comparison completers and non-completers	Y/N/?	Positive if article mentions that there are no significant differences between participants who completed the study and who did not, concerning key characteristics gender, age and pre-existing pain and candidate predictors and outcome, or there was no loss to follow-up. Negative if there are clear differences.
Predictor measurement			
P1	Definition of predictors	Y/?	Positive if the article clearly defines or describes all candidate predictors (concerning *both* clinical and demographic features).
P2	Measurement of predictors reliable and valid	Y/N/?	Positive if ≥1 candidate predictors are measured in a valid and reliable way, or referral is made to other studies which have established reliability and validity.
P3	Coding scheme and cut-off points	Y/N/?	Positive if coding scheme for candidate predictors were defined, including cut-off points and rationale for cut-off points was given; or if there was no dichotomization or classification. Negative when median is used as cut-off point.
P4	Data presentation	Y/N/?	Positive if frequencies or percentages or mean (SD/CI), or median (IQR) are reported of all candidate predictors.
Outcome measurement			
O1	Outcome(s) defined	Y/N/?	Positive when a clear definition of the outcome(s) of interest is presented.
O2	Measurement of outcome(s) reliable and valid	Y/N/?	Positive when outcome is measured in a valid and reliable way, or there is referred to other studies which have established reliability and validity.
O3	Coding scheme and cut-off points described	Y/N/?	Positive if coding scheme of the outcome was defined, including cut-off points and rationale for cut-off points was given; or if there was no dichotomization.
O4	Appropriate end-points of observation	Y/N/?	Positive if observation was obtained at a fixed moment after inclusion, negative when variable observation moments where used between patients.
O5	Data presentation	Y/N/?	Positive if frequencies or percentages or mean (SD/CI) or median (IQR) are reported of one of the main outcome measure.
Statistical analysis			
S1	Strategy for model building described	Y/N/?	Positive if the method of the selection process for multivariable analysis is presented (e.g. forward, backward selection, including p-value).
S2	Sufficient sample size	Y/N/?	Positive if in logistic regression analysis number of patients with a positive or negative outcome (event) per variable is adequate, i.e. is equal to or exceeds 10 events per variable in the multivariable model (EPV), or in case of linear regression analysis, N is ≥100.
S3	Presentation univariable analysis	Y/N/?	Positive if univariable crude estimates and confidence intervals (β/SE, OR/CI, RR, HR) are reported. Negative when only p-values or correlation coefficients are given, or if no tests are performed at all.
S4	Presentation multivariable analysis	Y/N/?	Positive if for the multivariable models point estimates with confidence intervals (β/SE, OR/CI, RR, HR,) are reported.
S5	Continuous predictors	Y/N/?	Positive if continuous predictors are not dichotomized in the multivariable model.
Clinical performance/validity			
C1	Clinical performance	Y/?	Positive if article provides information concerning ≥1 of the following performance measures: discrimination (e.g. ROC), calibration (e.g. HL statistic), explained variance, clinical usefulness (e.g. sensitivity, specificity, PPV, NPV)
C2	Internal validation	Y/N/?	Positive if appropriate techniques are used to assess internal validity (e.g. cross-validation, bootstrapping), negative if split-sample method was used.
C3	External validation	Y/?	Positive if the prediction model was validated in a second independent group of comparable patients.

Y, Positive, 1 point; N, Negative, 0 points; ?, Partial/unknown

1. Veerbeek JM, Kwakkel G, van Wegen EE, Ket JC, Heymans MW. Early prediction of outcome of activities of daily living after stroke: a systematic review. Stroke 2011;42:1482-1488.

Supplementary Table III: Characteristics and predictors for persistence of neuropathic pain of included low-quality studies

Art	Qas	Patient group	Study design	Definition PNP + follow-up	Statistical analysis	Predictors/Non-Predictors	Effect	95% CI	Measurement
Postherpetic Neuralgia (PHN)									
Beutner 1995 (1)	17	N=1141; mean age 68 yrs; 56,8% female	RCT	PHN after rash healing or 30 days	Cox's proportional hazards model	**Predictors** Older age Higher severity of acute pain Presence of prodromal pain	HR 1.42 HR 3.00 HR 1.30	1.20-1.67 2.26-3.99 1.06-1.56	>60 yrs Mild vs. severe pain
						Non-Predictors Female gender Treatment within 48 hours of rash onset	HR 0.94 HR 0.91	0.82-1.09 0.79-1.05	
Katz 2005 (2)	17	N=20 (PHN: mean age 63,2 yrs, 55% female); N=82 (no PHN: mean age 59,2, 56,1% female)	COH P	Nonzero pain intensity at 3.5 months (PHN)	Forward multiple logistic regression analysis	**Predictors** Older age Poorer role functioning Greater personality disorder symptoms Greater interference in physical health	OR 1.07 OR 2.34 OR 1.09 OR 1.16	1.01-1.12 1.34-4.08 1.01-1.18 1.01-1.34	MOS Pain Index PDQ-R MHLC
						Non-Predictors Duration of herpes zoster Immune status Presence of a prodrome Physical health defined as the total number of medical conditions and aliments Acute pain intensity	OR 0.97 OR 1.59 OR 2.21 OR 1.11 OR 0.95	0.88-1.07 0.07-5.04 0.54-9.15 0.93-1.32 0.69-1.32	Life stressors and social resources inventory
Haanpaa 2000 (3)	16	N=113; mean age 58 yrs; 63 female	COH P	Any zoster-associate pain at 3 months from rash onset	Multivariate logistic regression analysis	**Predictors** Older age Pinprick hypoesthesia baseline Brush-evoked allodynia Stretch-evoked allodynia	OR 1.06 OR 7.72 OR 5.89 OR 4.13	1.00-1.09 2.00-29.90 1.50-23.10 0.98-17.50	Increasing age Sharp wooden stick Stretching of skin
						Non-Predictors Gender Location of rash Rash severity Compression-evoked allodynia Moderate/severe acute pain	- - - - -	- - - - -	
Coen 2006 (4)	16	N=280	COH P	VAS≥3 3 or 6 months after HZ	Multivariate analysis	**Predictors** Age > 50 yrs Female sex Pain severity as VAS>5 Ophthalmic involvement	OR 3.9 (3m) / OR 13.8 (6m) OR 5.21 (6m) OR 3.9 (3m) / OR 3.7 (6m) OR 3.2 (3m) / OR 5.3 (6m)	1.38-11.1 1.74-110.0 1.38-19.6 1.33-11.5 1.01-13.5 1.19-8.55 1.66-16.9	VAS
						Non-Predictors *PHN at 3 months* Female gender Prodromal pain Extent of rash score Time from onset of rash PHN at 6 months Prodromal pain Extent of rash	 OR 2.45 - - OR 0.93 - -	 0.96-6.23 - - 0.80-1.07 - -	

Supplementary Table III (cont): Characteristics and predictors for persistence of neuropathic pain of included low-quality studies

Art	Qas	Patient group	Study design	Definition PNP + follow-up	Statistical analysis	Predictors/Non-Predictors	Effect	95% CI	Measurement
Drolet 2010 (5)	16	N=249; mean age 65 yrs; 58% female	COH P	Worst pain ≥3, persisting 90 days after rash onset	Log-binomial regression	**Predictors** Older age Higher pain severity baseline (severe pain ≥7) Problems with usual activities before having HZ	 RR 1.03 RR 2.06 RR 1.92	 1.01-1.05 0.98-4.35 1.20-3.09	 Age at rash onset ZBPI EQ-5D
						Non-Predictors Gender Education Working Lower income Has another pain condition Being anxious or depressed EQ-5D index score before HZ VAS score before HZ Primary dermatome affected Number of lesions Worst pain Prodromal pain Duration of prodromal pain Has taken antiviral medication Adequacy of antiviral treatment Other medication	- (uni) - (uni) - (uni) RR 1.85 - (uni) - (uni) - (uni) - (uni) - (uni) - (uni) - (uni) - (uni) - (uni) - (uni) - (uni) - (uni)	- - 0.89-3.83 - - - - - - - - - - - - -	
Haythornwaite 2003 (6)	16	N=103; mean age 71 yrs; 55% female	RCT	Pain after 2 months (PHN)	Forward hierarchical regression	**Predictors** Catastrophizing at baseline Pain severity at baseline	 OR 1.36$ OR 1.57$$	 - -	 CSQ NRS 0-10
						Non-Predictors Overall activity level Depressive symptoms Coping strategies Coping self-statements Diverting attention Ignoring sensations Reinterpreting sensations Praying and hoping Increasing activity	OR 0.92$$$ - - - - - - - -	- - - - - - - - -	 Coping strategies questionnaire
Opstelten 2002 (7)	16	N=837	COH R	Pain persisting 1 or 3 months after HZ diagnosis	Multivariate logistic regression analysis	**Predictors** Older age 55-74 years Older age >75 years Ophthalmic localization	OR 4.2 (1m) / OR 5.4 (3m) OR 10.7 (1m) OR 19.7 (3m) OR 2.1 (1m)	1.8-9.7 1.1-26.5 4.6-25.1 4.3-90.9 1.0-4.6	55-74 years >75 years
						Non-Predictors Gender Diabetes Use of psychopharma Painful prodrome Ophthalmic localization	OR 0.8 (1m) OR 1.0 (3m) OR 1.4 (1m) OR 1.7 (3m) OR 1.4 (1m) OR 1.4 (3m) OR 2.1 (1m) OR 1.2 (3m) OR 2.3 (1m) OR 2.2 (3m)	0.4-1.5 0.9-1.0 0.6-3.8 0.5-6.2 0.5-3.9 0.3-5.6 0.9-5.2 0.3-5.6 1.1-4.6 0.3-5.6	

Supplementary Table III (cont): Characteristics and predictors for persistence of neuropathic pain of included low-quality studies

Art	Qas	Patient group	Study design	Definition PNP + follow-up	Statistical analysis	Predictors/Non-Predictors	Effect	95% CI	Measurement
Decroix 2000 (8)	15	N=1191	COH P	Not completely specified, follow-up was until 6 months (PHN)	Cox's proportional hazards model	**Predictors** Older age Higher pain severity baseline Higher intensity prodromal pain	HR 1.91 - HR 1.78	1.71-2.12 - 1.53-2.07	18-50 yrsvs ≥50yrs Moderate/severe Severe/very severe vs non/mild
						Non-Predictors Zoster type Concomitant neurological disorders Presence of prodromal pain Abnormal sensations prior to study entry Time from rash onset and start of treatment	- HR 1.10 - -	- 0.92-1.33 - -	
Harding 1987 (9)	15	N=71; mean age 63,2 yrs; 45 female	COH P	Presence of continuous or frequent pain at or after 6 months (PHN)	Paired t-test	**Predictors** Older age Higher VAS-score >60 yrs	*P*<0.05 *P*<0.05	- -	>70 yrs VAS 100mm
						Non-Predictors Gender Ocular involvement Nasociliary nerve involvement Longer rash duration Higher rash severity	*P*>0.05 *P*>0.5 *P*>0.1 *P*>0.05 *P*>0.1		
Kurokawa 2002 (10)	15	N=263; mean age 59 yrs; 136 female	COH P	Pain after 3 months (PHN)	Unpaired t-test	**Predictors** Older age Hypoesthesia Disturbed sleep	*P* <0.01 *P*<0.01 *P*<0.01		≥ 60 yrs
						Non-Predictors Gender Affected region Underlying disease Immunodeficiency Erosion Ulcer Scar Generalized rash Allodynia Grade of erythema Concomitant medications	- - - - - - - - - - - -	- - - - - - - - - - - -	
Petersen 2010 (11)	15	N=94; PHN: median age 70 yrs, 57% female; no PHN: median age 67 yrs, 59% female	COH P	Pain 6 months after rash onset	Mixed effects backward regression model	**Predictors** Higher average daily pain baseline Cold detection asymmetry	OR 1.8 OR 1.18	1.2-2.6 1.03-1.35	VAS 100mm last 48h TSA II thermal sensory analyzer
						Non-Predictors Allodynia Thermal sensory asymmetry Warm detection asymmetry Heat pain detection asymmetry Total capsaicin response	- - - - -	- - - - -	TSA II thermal sensory analyzer

Supplementary Table III (cont): Characteristics and predictors for persistence of neuropathic pain of included low-quality studies

Art	Qas	Patient group	Study design	Definition PNP + follow-up	Statistical analysis	Predictors/Non-Predictors	Effect	95% CI	Measurement
Nurmikko 1990 (12)	15	N=31; mean age 62.2 yrs; 18 female	COH P	Pain after 3 months (PHN)	Forward logistic regression analysis	**Predictors** Thermal threshold abnormalities	OR 12.3	1.19-126.77	Marstock method
						Non-Predictors Age Gender Vibration asymmetry Mechanical allodynia Treatment	- - - - -	- - - - -	
Dworkin 1992 (13)	14	N=19; mean age 62.6 yrs, 9 female	COH P	Pain after 3 months (PHN)	Chi square tests, t-tests, two-tailes Mann-Whitney U test	**Predictors** Higher trait and state anxiety Greater depression Lower life satisfaction Greater disease conviction Higher acute pain severity	t 2.90 t 2.43 t 2.27 t 3.43 t 2.55	- - - - -	STAI BDI LSES IBQ MPQ
						Non-Predictors Dysfunctional attitudes Hypochondriasis Psychological versus somatic focusing Affective inhibition Affective disturbance Denial Irritability Stressful life events	t 0.47 t 1.25 t 0.30 t 0.37 t 1.66 t 0.47 t 0.77 t 1.36	- - - - - - - -	IBQ IBQ IBQ IBQ IBQ IBQ
Haanpaa 1999 (14)	14	N=103; mean age 65 yrs; 73 female	COH P	Pain persisting at least 3 months from rash onset (PHN)	Multivariate logistic regression analysis	**Predictors** Pinprick hypoesthesia baseline Brush-evoked allodynia Stretch –evoked allodynia Warm threshold elevation Tactile threshold elevation	OR 11.70 OR 6.84 OR 8.71 OR 9.10 OR 5.76	2.50-54.80 1.44-32.40 1.54-49.20 1.71-48.40 1.23-26.90	QST QST QST SOMEDIC Thermotest Semmes-Weinstein
						Non-Predictors Age Gender Location of rash Rash severity Compression-evoked allodynia Cold threshold elevation Heat pain threshold reduction Moderate/severe acute pain	- - - - - - - -	- - - - - - - -	
Jung 2004 (15)	14	N=855; mean age 52,3 yrs, 51.7% female	Follow-up data of 2 RCT's	Pain after 4 months (PHN)	Forward logistic regression analysis	**Predictors** Older age Female sex Presence of prodrome Higher severe acute pain Severe rash	OR 1.03# OR 2.01## OR 2.75### OR 2.11#### OR 3.00#####	1.01-1.05 1.28-3.16 1.18-6.37 1.35-3.32 1.88-4.81	Pain before rash onset Lesion count
						Non-Predictors Rash duration	OR 0.84#######	0.64-1.11	

Supplementary Table III (cont): Characteristics and predictors for persistence of neuropathic pain of included low-quality studies

Art	Qas	Patient group	Study design	Definition PNP + follow-up	Statistical analysis	Predictors/Non-Predictors	Effect	95% CI	Measurement
Wilson 2013 (16)	13	N=470; mean age 52.8 yrs; 100% female	COH R	Postoperative neuropathic pain within 1 year after breast surgery	Multivariate Logistic regression	**Predictors** African American race Diabetes Mellitus Fybromyalgia Taxane-based chemotherapy	OR 1.78 OR 2.21 OR 2.75 OR 2.85	- 3.17 1.18 - 4.15 1.13 - 6.69 1.23 - 6.58	
						Non-Predictors Asian race Hispanic race Type of surgery Axillary surgery Radiation therapy	OR 0.61 OR 1.45 OR 1.37 OR 1.32 OR 1.62	0.10 - 3.53 0.05 - 39.9 0.71 - 2.66 0.64 - 2.71 0.92 - 2.85	
Leplow 1990 (17)	13	N=39; mean age PHN 64.4 years, non-PHN 55.6 years; n female: PHN 16, non-PHN 8	Retrospective cross-sectional study	Duration (?) Post herpetic neuralgia defined as pain 4 weeks after resolution skin lesions	Multivariate analysis of variance, multiple regression analysis (?), t-test (?), chi-square test	**Predictors** Remission time Psychopathological impairment on psychopathological index **Non-Predictors** Gender Age Treatment latency Stationary treatment Subjective pain and sensory signs at onset Localization PHN Co-morbidity (lethal or "chronic") Psychosocial variables	Beta 0.63, P <0.001 Beta (?) 0.50 - - - - - - - -	-	Duration (?) pain VAS and McGill
Thyregod 2007 (18)	12	N=94 (PHN: median age 70.5 yrs 57% female; no PHN: median age 67 yrs, 59% female)	COH P	Pain 6 months after rash onset	Mixed effects regression model	**Predictors** Higher affective distress Higher number of analgesics taken Higher average daily pain at study entry Higher percentage of affected dermatomes in cervical and lumbar region SF-MPQ descriptor 'sharp'	- - - - -	- - - - -	MPI VAS 100 mm SF-MPQ
						Non-Predictors Prodromal pain Rash severity Antiviral treatment Taking any analgesic Coping strategies Pain interference Life control Support Negative responses Solicitous responses Distracting responses Household chores Outdoor work Outdoor activities Social activities	- - - - - - - - - - - - - - -	- - - - - - - - - - - - - - -	MPI MPI MPI MPI MPI MPI MPI MPI MPI MPI

Supplementary Table III (cont): Characteristics and predictors for persistence of neuropathic pain of included low-quality studies

Art	Qas	Patient group	Study design	Definition PNP + follow-up	Statistical analysis	Predictors/Non-Predictors	Effect	95% CI	Measurement
Whitley 1999 (19)	12	N=201; median age 61 yrs, 51% female	RCT	Pain after 1 month (PHN)	Risk ratios (RR)	**Predictors** Intense pain at presentation and ≥47 lesions at baseline	RR 2.4	1.01-5.9	Mild/moderate/severe
						Non-Predictors Treatment of herpes zoster	-	-	
Baron 1997 (20)	11	N=34; mean age PHN 68.6 yrs, mean age non-PHN 67.2 yrs	COH P	Pain after 6 months (PHN)	U-tests	**Predictors** High vibration detection thresholds	*P*<0.05	SEM 10.9	Vibratester
						Non-Predictors Age Acute pain severity Cutaneous nociceptive C-fiber function Parasympathetic function	*P*>0.05 *P*>0.05 *P*>0.05 *P*>0.05	- - - -	Flare reaction
Choo 1997 (21)	11	N=821	COH R	Presence of pain and other documented sensory symptoms in the zoster dermatome more than 30 or 60 days after the onset of HZ for which no other cause was registered	Cross-tabulations and simple logistic regression models	**Predictors** Older age Prodromal symptoms Comorbidities other than cancer and diabetes	PR 14.7 (30d) / PR 27.4 (60d) PR 2.1 (30d) / PR 3.4 (60d) PR 9.5 (60d)	6.8-32.0 / 8.8-85.4 1.1-4.3 / 1.3-9.1 2.0-45.9	≥50 years
						Non-Predictors Female gender Affected dermatome Interference with activities of daily living Diabetes Cancer Complications Use of acyclovir Use of corticosteroids before HZ Use of corticosteroids after HZ	PR 1.3 (30d) / PR 0.9 (60d) - PR 1.7 (30d) / PR 1.3 (60d) PR 2.1 (30d) / PR 2.7 (60d) PR 0.2 (30d) / PR 0.1 (60d) - PR 2.9 (30d) / PR 1.4 (60d) PR 1.7 (30d) / PR 0.7 (60d)	0.6-2.7 / 0.4-2.3 - 0.7-4.5 / 0.4-4.2 0.6-7.7 / 0.4-17.9 0.1-0.8 / 0.02-0.9 - 0.7-11.3 / 0.3-6.0 0.6-4.3 / 0.2-2.8	
Nagasako 2002 (22)	11	N=1778	Data from 4 RCT's	Pain present in the affected area 3 months after rash onset	Logistic regression analysis	**Predictors** Greater rash severity	-	-	
						Non-Predictors -	-	-	
Quinlivan 2007 (23)	11	N=130; age ≤50 N=55, age >50 N=75; 64 female	COH P	Pain after 6 and 12 weeks (PHN)	Stepwise logistic regression analysis	**Predictors** Older age Female sex Immunosuppression	*P*=0.001 (6w) / *P*=0.005 (12w) *P*=0.054 (6w) / *P*=0.097 (12w) *P*=0.002 (6w)		≤50 vs. >50 years
						Non-Predictors Unknown	-		

Supplementary Table III (cont): Characteristics and predictors for persistence of neuropathic pain of included low-quality studies

Art	Qas	Patient group	Study design	Definition PNP + follow-up	Statistical analysis	Predictors/Non-Predictors	Effect	95% CI	Measurement
Zaal 2000 (24)	11	N=81; median age 66 yrs; 44 female	COH P	Pain after 2 months (PHN)	Fisher's exact test	**Predictors** Older age Moderate to severe acute neuralgia Moderate to severe rash extent Moderate to severe rash manifestation Non-trigeminal cranial nerve involvement Ocular inflammation	p=0.003 p=0.00001 p=0.03 p=0.00009 p=0.019 p=0.0003	- - - - - -	Mild/moderate/severe Mild/moderate/severe with photography
						Non-Predictors Gender	p=0.53	-	
Meister 1998 (25)	10	N=635; 56% female	COH P	Presence of pain in the afflicted area 4-5 weeks after HZ	Multivariate logistic regression analysis	**Predictors** Older age Female sex Intense pain at presentation Symptoms in prodromal phase >50 hemorrhagic lesions Affliction in cranial/sacral area of the rash	p=0.002 p=0.004 p=0.001 p=0.03 p=0.0.04	- - - - -	
						Non-Predictors Disease history Higher body temperature Nocturnal sweating Nonspecific pain Paresthesias Fatigue Nausea Lymph node swelling Extension of lesions Therapy before first visit	- - - - - - - - - -	- - - - - - - - - -	
Bruxelle 1995 (26)	9	N=301; mean age 55yrs	COH P	Pain after 6 months	Not specified	**Predictors** Older age Higher pain severity at baseline Presence of neurological deficit (hypoesthesia or anesthesia)	p<0.001 p<0.02 p<0.001	- - -	>70 years Mild/moderate/severe
						Non-Predictors -	-	-	
Goh 1997 (27)	9	N=164; mean age 48,8 yrs; 49% female	COH R	Pain persisting 4 weeks after the appearance of blistering eruptions	Chi square, Fisher exact test and tests for equality of variance	**Predictors** Older age	p=0.011	-	>50 yrs
						Non-Predictors Female gender	-	-	

Supplementary Table III (cont): Characteristics and predictors for persistence of neuropathic pain of included low-quality studies

Art	Qas	Patient group	Study design	Definition PNP + follow-up	Statistical analysis	Predictors/Non-Predictors	Effect	95% CI	Measurement
Quinlivan 2011 (28)	9	N=63; age≤50 yrs: 57% males; age >50 yrs: 51% males	COH P	Longer time to recovery from PHN (pain measurements at 1, 3 and 6 months)	Multivariate cox proportional hazards regression	**Predictors** Taking antivirals during acute HZ	HR 2.077	1.052 - 4.101	5-degree semi-quantitative scale
						Higher pain severity at baseline	HR 0.846	0.723 - 0.991	
						Presence of prodromal symptoms	HR 3.171	1.571 - 6.398	
						Being immunocompromised	HR 2.758	1.034 - 7.355	
						Non-Predictors Age	HR 0.988	0.973-1.003	
						Gender	HR 0.915	0.502-1.667	
						Rash duration at baseline	HR 0.937	0.840-1.046	
						Disseminated rash	HR 1.687	0.600-4.737	
						Trigeminal involvement	HR 1.266	0.562-2.851	
						Allodynia	HR 1.467	0.651-3.305	
						Viral load	HR 0.679	0.400-1.153	
Zak-Prelich 2003 (29)	9	N=30; meanage 55,4 yrs	COH P	Presence of pain more than 4 weeks after the lesions have resolved (PHN)		**Predictors** Age	-	-	
						Non-Predictors -	-	-	
Riopelle 1984 (30)	8	N=72	COH P	Pain 6 months or more after the first symptoms of herpes zoster		**Predictors** Older age	-	-	≥60 yrs
						Severe initial neuralgia	-	-	
						Non-Predictors Unknown	-	-	
Scott 2003 (31)	8	N=204; 103 female	COH P	Pain after 3 months (PHN)	Effects of individual parameters on the likelihood of developing PHN	**Predictors** Older age	-	-	>50 years
						Higher acute pain severity	-	-	VAS
						Non-Predictors Severity of prodromal pain	-	-	
						Duration of prodromal pain	-	-	
McKendrick 2009 (32)	6	N=158; mean age 71.7 yrs; 79 female	COH P	Pain after 9 years (pain in last year vs. no pain in last year) (PHN)	Fisher's exact test	**Predictors** Female sex	*P*=0.046	-	Lesion count
						Moderate or severe acute pain	*P*=0.006	-	
						Severity of rash	*P*=0.033	-	
						Non-Predictors Rash duration	-	-	
						Prodromal pain >72h before rash	*P*=0.49	-	
						Treatment	*P*=0.44	-	
Radicularpain& sciatica									
Peul 2008 (33)	19	N=283; mean age female (32%) 42,9 yrs, mean age men 42,4 yrs	RCT	Unsatisfactory outcome of sciatic pain after 12 months	Backward multivariate logistic regression analysis	**Predictors** Female sex	OR 2.81	1.38 - 5.74	
						Smoking	OR 2.01	0.99 - 4.1	
						Surgery	OR 0.49	0.24 - 1.00	Versus conservative
						Positive Bragard's test	OR 2.72	1.33 - 5.58	Maximal straight leg raising

Supplementary Table III (cont): Characteristics and predictors for persistence of neuropathic pain of included low-quality studies

Art	Qas	Patient group	Study design	Definition PNP + follow-up	Statistical analysis	Predictors/Non-Predictors	Effect	95% CI	Measurement
						Non-Predictors			
						Older age	OR 1.76 (uni)	0.89-3.47	
						Having a mentally demanding job	OR 1.06	0.44-2.53	
						Physical job			
						Having a partner	OR 1.16 (uni)	0.59-2.29	
						Having children	OR 0.69 (uni)	0.34-1.38	
						Being a housewife	OR 1.26 (uni)	0.63-2.52	
						Acute start of sciatica	OR 1.72	0.52-5.65	
						Sciatica provoked by sitting	OR 0.91 (uni)	0.47-1.77	
						Sciatica provoked by sneeze	OR 1.26	0.50-3.20	
						Crossed leg raising	OR 0.77 (uni)	0.39-1.52	
						Straight leg raising	OR 1.75	0.82-3.77	
						VAS leg pain>70mm	OR 0.91 (uni)	0.44-1.89	
						Sensory disturbance	OR 1.39 (uni)	0.73-2.62	
							OR 1.73 (uni)	0.50-6.00	
Miranda 2002 (34)	9	N=3312	COH P	Persistent sciatic pain	Logistic regression model	**Predictors**			
						Poor job satisfaction	OR 2.8	1.2-6.7	
						Being an ex-smoker	OR 2.3	1.3 - 4.3	
						Moderate or actively jogging	OR 3.9	1.4 – 10.7	
						Mental stress (much)	OR 2.8	1.2 - 6.7	
						Non-Predictors			
						Older age	OR 2.0	0.5 - 7.9	
						Female gender	OR 1.0	0.6-1.8	
						Current smoker	OR 1.0	0.5-1.9	
Postsurgical pain									
Alves Nogueira 2012 (35)	12	N=203; mean age 58 years; 100% women	COH P	PMPS defined as intercostobrachial pain, neuroma or phantom breast pain after 6 months	Logistic regression, enter method	**Predictors**			
						Younger age	RR 5.22	1.11-24.64	
						Axillary surgical approach with >15 removed lymph nodes	RR 2.01	1.08-3.75	
						Non-Predictors			
						Higher body mass index	-	-	
						Employment	-	-	
						Altered psychological profile	-	-	
						Movement restriction	-	-	
						Type of surgery	-	-	
						Treatment	-	-	
Duale 2011 (36)	9	N=73; mean age 59.6 yrs; 70% males	COH P	Pain 4 months after surgery		**Predictors**			
						Younger age	-	-	
						Female sex	-	-	
						Spontaneous pain	-	-	
						Non-Predictors			
						Use of perioperative ketamine	-	-	
						Use of anticancer chemotherapy	-	-	
						Allodynia	-	-	
						Hyperalgesia	-	-	
						Hypo-anesthesia	-	-	

Supplementary Table III (cont): Characteristics and predictors for persistence of neuropathic pain of included low-quality studies

Art	Qas	Patient group	Study design	Definition PNP + follow-up	Statistical analysis	Predictors/Non-Predictors	Effect	95% CI	Measurement
Searle 2009 (37)	9	N=100; mean age 62 yrs; 64% male	COH P	Pain 3 months after surgery	Stepwise logistic regression analysis	**Predictors** Acute NP Pain-like strange and unpleasant sensations	RR 3.5 RR 4.5	1.7-7.2 2.3-8.7	NRS 0-10 S-LANSS
						Non-Predictors Older age Gender Type of operation Malignant or benign disease Analgesic technique Neuropathic symptoms and signs	- - - - - -	- - - - - -	S-LANSS
Other									
Gehling 2003 (38)	9	N=42; mean age 57 years; 31 females	Retrospective cross-sectional study	Complex regional pain syndrome I and II, IASP-Orlando criteria.	Odds ratio Fischer exact test	**Predictors** Younger age	OR 4.00	1.04-15.26	Limited or partial improvement pain (<50%) vs. good to excellent improvement pain (≥50%)
						Non-Predictors Gender Duration anamnesis Pre treatment VAS Pain intensity Guanethidin treatment Treatment duration			
Attal 2009 (39)	12	N=48; mean age 57 yrs; 15 female	COH P	Chronic neuropathy after 12 months after use of neurotoxins	Logistic regression analysis	**Predictors** NPSI total score (≥9/100) Duration of cold-evoked symptoms (≥4 days)	OR 25.00 OR 22.00	1.80-346.78 1.54-314.74	NPSI NPSI
						Non-Predictors Older age Gender Type of chemotherapy Oxaliplatin dosages Intensity of cold-evoked pain	OR 7.0 OR 1.0 OR 0.25 OR 1.4 OR 10.0	0.61-79.89 0.14-7.10 0.03-1.99 0.18-11.08 0.85-117.04	

Articles ordered according to their methodological quality score.
Art: article; Qas: Quality assessment (/27); NP: Neuropathic Pain; HZ: Herpes Zoster; PHN: Post Herpetic Neuralgia; PMPS: Post-mastectomy pain syndrome; PPSP: Persistent Postsurgical Pain; HR: Hazard ratio; OR: Odds ratio; RR: Relative risk; B: regression coefficient; PR: Prevalence ratios; RCT: Randomized Controlled Trial; COH P: prospective cohort; COH R: retrospective cohort; SF-MPQ: Short Form McGill Pain Questionnaire; ZBPI: Zoster Brief Pain Inventory; S-LANSS: Leeds Assessment of Neuropathic Symptoms and Signs; NRS: Numerical Rating Scale; VAS: Visual Analogue Scale; MPI: Multidimensional pain inventory; PDQ-R: Personality Disorder Questionnaire-Revised; MHLC: Multidimensional Health Locus of Control scale; CSQ: Coping Strategies Questionnaire; QST: Quantitative Sensory Testing; STAI: State-Trait Anxiety Inventory; BDI: Beck Depression Inventory; LSES: Life Satisfaction in the Elderly Scale; IBQ: Illness Behavior Questionnaire; NPSI: Neuropathic Pain Symptom Inventory. Uni: only results of univariate analysis
Own calculations based on .# B 0.03, SE 0.01; ## B 0.7, SE 0.23; ### B 1.01, SE 0.43; #### B 0.75, SE 0.23; ##### B 1.1, SE 0.24;###### B -0.17, SE 0.14; $ B 0.31; $$ B 0.45, ^ B 2.51, SE 1.19.

References

1. Treede RD, Jensen TS, Campbell JN, Cruccu G, Dostrovsky JO, Griffin JW, Hansson P, Hughes R, Nurmikko T, Serra J. Neuropathic pain: Redefinition and a grading system for clinical and research purposes. *Neurology* 2008; 70:1630-1635.
2. Baron R. Mechanisms of disease: Neuropathic pain--a clinical perspective. *Nat Clin Pract Neurol* 2006; 2:95-106.
3. Harden RN. Chronic neuropathic pain. Mechanisms, diagnosis, and treatment. *Neurologist* 2005; 11:111-122.
4. Vissers KC. The clinical challenge of chronic neuropathic pain. *Disabil Rehabil* 2006; 28:343-349.
5. Woolf CJ, Mannion RJ. Neuropathic pain: Aetiology, symptoms, mechanisms, and management. *Lancet* 1999; 353:1959-1964.
6. Freynhagen R, Bennett MI. Diagnosis and management of neuropathic pain. *BMJ* 2009; 339:b3002.
7. Smith BH, Torrance N, Bennett MI, Lee AJ. Health and quality of life associated with chronic pain of predominantly neuropathic origin in the community. *Clinical Journal of Pain* 2007; 23:143-149.
8. Arning K, Baron R. Evaluation of symptom heterogeneity in neuropathic pain using assessments of sensory functions. *Neurotherapeutics* 2009; 6:738-748.
9. Jay GW, Barkin RL. Neuropathic pain: Etiology, pathophysiology, mechanisms, and evaluations. *Dis Mon* 2014; 60:6-47.
10. Baron R, Binder A, Wasner G. Neuropathic pain: Diagnosis, pathophysiological mechanisms, and treatment. *Lancet Neurol* 2010; 9:807-819.
11. Boogaard S, Heymans MW, Patijn J, de Vet HC, Faber CG, Peters ML, Loer SA, Zuurmond WW, Perez R. Predictors for persistent neuropathic pain--a Delphi survey. *Pain Physician* 2011; 14:559-568.
12. Boogaard S, de Vet HC, Faber CG, Zuurmond WW, Perez RS. An overview of predictors for persistent neuropathic pain. *Expert Rev Neurother* 2013; 13:505-513.
13. Veerbeek JM, Kwakkel G, van Wegen EE, Ket JC, Heymans MW. Early prediction of outcome of activities of daily living after stroke: A systematic review. *Stroke* 2011; 42:1482-1488.
14. Bornman J. The World Health Organisation's terminology and classification: Application to severe disability. *Disabil Rehabil* 2004;26:182-188.
15. Stucki G. International Classification of Functioning, Disability, and Health (ICF): A promising framework and classification for rehabilitation medicine. *Am J Phys Med Rehabil* 2005; 84:733-740.
16. Dworkin RH, Hartstein G, Rosner HL, Walther RR, Sweeney EW, Brand L. A high-risk method for studying psychosocial antecedents of chronic pain: The prospective investigation of herpes zoster. *J Abnorm Psychol* 1992; 101:200-205.
17. Miranda H, Viikari-Juntura E, Martikainen R, Takala EP, Riihimaki H. Individual factors, occupational loading, and physical exercise as predictors of sciatic pain. *Spine (Phila Pa 1976)* 2002; 27:1102-1109.
18. Attal N, Bouhassira D, Gautron M, Vaillant JN, Mitry E, Lepere C, Rougier P, Guirimand F. Thermal hyperalgesia as a marker of oxaliplatin neurotoxicity: A prospective quantified sensory assessment study. *Pain* 2009; 144:245-252.
19. Choo PW, Galil K, Donahue JG, Walker AM, Spiegelman D, Platt R. Risk factors for postherpetic neuralgia. *Arch Intern Med* 1997; 157:1217-1224.
20. Duale C, Guastella V, Morand D, Cardot JM, Aublet-Cuvelier B, Mulliez A, Schoeffler P, Escande G, Dubray C. Characteristics of the neuropathy induced by thoracotomy: A 4-month follow-up study with psychophysical examination. *Clinical Journal of Pain* 2011; 27:471-480.
21. Johansen A, Romundstad L, Nielsen CS, Schirmer H, Stubhaug A. Persistent postsurgical pain in a general population: Prevalence and predictors in the Tromso study. *Pain* 2012; 153:1390-1396.
22. Masselin-Dubois A, Attal N, Fletcher D, Jayr C, Albi A, Fermanian J, Bouhassira D, Baudic S. Are psychological predictors of chronic postsurgical pain dependent on the surgical model? A comparison of total knee arthroplasty and breast surgery for cancer. *J Pain* 2013; 14:854-864.
23. Peul WC, Brand R, Thomeer RT, Koes BW. Influence of gender and other prognostic factors on outcome of sciatica. *Pain* 2008; 138:180-191.
24. Searle RD, Simpson MP, Simpson KH, Milton R, Bennett MI. Can chronic neuropathic pain following thoracic surgery be predicted during the postoperative period? *Interact Cardiovasc Thorac Surg* 2009; 9:999-1002.
25. Coen PG, Scott F, Leedham-Green M, Nia T, Jamil A, Johnson RW, Breuer J. Predicting and preventing post-herpetic neuralgia: Are current risk factors useful in clinical practice? *Eur J Pain* 2006; 10:695-700.
26. Drolet M, Brisson M, Schmader K, Levin M, Johnson R, Oxman M, Patrick D, Camden S, Mansi JA. Predictors of postherpetic neuralgia among patients with herpes zoster: A prospective study. *J Pain* 2010; 11:1211-1221.
27. Harding SP, Lipton JR, Wells JC. Natural history of herpes zoster ophthalmicus: Predictors of postherpetic neuralgia and ocular involvement. *Br J Ophthalmol* 1987; 71:353-358.
28. Katz J, McDermott MP, Cooper EM, Walther RR, Sweeney EW, Dworkin RH. Psychosocial risk factors for postherpetic neuralgia: A prospective study of patients with herpes zoster. *J Pain* 2005; 6:782-790.
29. Opstelten W, Zuithoff NP, van Essen GA, van Loon AM, van Wijck AJ, Kalkman CJ, Verheij TJ, Moons KG. Predicting postherpetic neuralgia in elderly primary care patients with herpes zoster: Prospective prognostic study. *Pain* 2007; 132:S52-S59.
30. Goh CL, Khoo L. A retrospective study of the clinical presentation and outcome of herpes zoster in a tertiary dermatology outpatient referral clinic. *Int J Dermatol* 1997; 36:667-672.
31. Meister W, Neiss A, Gross G, Doerr HW, Hobel W, Malin JP, von EJ, Reimann BY, Witke C, Wutzler P. A prognostic score for postherpetic neuralgia in ambulatory patients. *Infection* 1998; 26:359-363.
32. Opstelten W, Mauritz JW, de Wit NJ, van Wijck AJ, Stalman WA, van Essen GA. Herpes zoster and postherpetic neuralgia: Incidence and risk indicators using a general practice research database. *Fam Pract* 2002; 19:471-475.
33. Parruti G, Tontodonati M, Rebuzzi C, Polilli E, Sozio F, Consorte A, Agostinone A, Di MF, Congedo G, D'Antonio D, Granchelli C, D'Amario C, Carunchio C, Pippa L, Manzoli L, Volpi A. Predictors of pain intensity and persistence in a prospective Italian cohort of patients with herpes zoster: Relevance of smoking, trauma and antiviral therapy. *BMC Med* 2010; 8:58.
34. Whitley RJ, Weiss HL, Soong SJ, Gnann JW. Herpes zoster: Risk categories for persistent pain. *J Infect Dis* 1999; 179:9-15.
35. McKendrick MW, Ogan P, Care CC. A 9 year follow up of post herpetic neuralgia and predisposing factors in elderly

patients following herpes zoster. *J Infect* 2009; 59:416-420.

36. Bouhassira D, Chassany O, Gaillat J, Hanslik T, Launay O, Mann C, Rabaud C, Rogeaux O, Strady C. Patient perspective on herpes zoster and its complications: An observational prospective study in patients aged over 50 years in general practice. *Pain* 2012; 153:342-349.
37. Haanpaa M, Laippala P, Nurmikko T. Allodynia and pinprick hypesthesia in acute herpes zoster, and the development of postherpetic neuralgia. *J Pain Symptom Manage* 2000; 20:50-58.
38. Haanpaa ML, Laippala PA, Nurmikko TJ. Thermal and tactile perception thresholds in acute herpes zoster. *Eur J Pain* 1999; 3:375-386.
39. Kurokawa I, Kumano K, Murakawa K. Clinical correlates of prolonged pain in Japanese patients with acute herpes zoster. *J Int Med Res* 2002; 30:56-65.
40. Nagasako EM, Johnson RW, Griffin DR, Dworkin RH. Rash severity in herpes zoster: Correlates and relationship to postherpetic neuralgia. *J Am Acad Dermatol* 2002; 46:834-839.
41. Nurmikko TJ, Rasanen A, Hakkinen V. Clinical and neurophysiological observations on acute herpes zoster. *Clin J Pain* 1990; 6:284-290.
42. Scott FT, Leedham-Green ME, Barrett-Muir WY, Hawrami K, Gallagher WJ, Johnson R, Breuer J. A study of shingles and the development of postherpetic neuralgia in East London. *J Med Virol* 2003; 70:S24-S30.
43. Bruxelle J. Prospective epidemiologic study of painful and neurologic sequelae induced by herpes zoster in patients treated early with oral acyclovir. *Neurology* 1995; 45:S78-S79.
44. Decroix J, Partsch H, Gonzalez R, Mobacken H, Goh CL, Walsh L, Shukla S, Naisbett B. Factors influencing pain outcome in herpes zoster: An observational study with valaciclovir. Valaciclovir International Zoster Assessment Group (VIZA). *J Eur Acad Dermatol Venereol* 2000; 14:23-33.
45. den Boer JJ, Oostendorp RA, Beems T, Munneke M, Evers AW. Continued disability and pain after lumbar disc surgery: The role of cognitive-behavioral factors. *Pain* 2006; 123:45-52.
46. Martinez V, Ben AS, Judet T, Bouhassira D, Chauvin M, Fletcher D. Risk factors predictive of chronic postsurgical neuropathic pain: The value of the iliac crest bone harvest model. *Pain* 2012; 153:1478-1483.
47. Beutner KR, Friedman DJ, Forszpaniak C, Andersen PL, Wood MJ. Valaciclovir compared with acyclovir for improved therapy for herpes zoster in immunocompetent adults. *Antimicrob Agents Chemother* 1995; 39:1546-1553.
48. Haythornthwaite JA, Clark MR, Pappagallo M, Raja SN. Pain coping strategies play a role in the persistence of pain in post-herpetic neuralgia. *Pain* 2003; 106:453-460.
49. Jung BF, Johnson RW, Griffin DR, Dworkin RH. Risk factors for postherpetic neuralgia in patients with herpes zoster. *Neurology* 2004; 62:1545-1551.
50. Leplow B, Lamparter U, Risse A, Wassilev SW. [Post-herpetic neuralgia: Clinical predictors and psychopathologic findings]. *Nervenarzt* 1990; 61:46-51.
51. Petersen KL, Rowbotham MC. Natural history of sensory function after herpes zoster. *Pain* 2010; 150:83-92.
52. Wilson GC, Quillin RC, III, Hanseman DJ, Lewis JD, Edwards MJ, Shaughnessy EA. Incidence and predictors of neuropathic pain following breast surgery. *Ann Surg Oncol* 2013; 20:3330-3334.
53. Dworkin RH, Portenoy RK. Pain and its persistence in herpes zoster. *Pain* 1996; 67:241-251.
54. Dieleman JP, Kerklaan J, Huygen FJ, Bouma PA, Sturkenboom MC. Incidence rates and treatment of neuropathic pain conditions in the general population. *Pain* 2008; 137:681-688.
55. Brandsborg B, Nikolajsen L, Hansen CT, Kehlet H, Jensen TS. Risk factors for chronic pain after hysterectomy: A nationwide questionnaire and database study. *Anesthesiology* 2007; 106:1003-1012.
56. Romundstad L, Breivik H, Roald H, Skolleborg K, Romundstad PR, Stubhaug A. Chronic pain and sensory changes after augmentation mammoplasty: Long term effects of preincisional administration of methylprednisolone. *Pain* 2006; 124:92-99.
57. Tasmuth T, Kataja M, Blomqvist C, von SK, Kalso E. Treatment-related factors predisposing to chronic pain in patients with breast cancer--a multivariate approach. *Acta Oncol* 1997; 36:625-630.
58. Trief PM, Grant W, Fredrickson B. A prospective study of psychological predictors of lumbar surgery outcome. *Spine (Phila Pa 1976)* 2000; 25:2616-2621.
59. Attal N, Rouaud J, Brasseur L, Chauvin M, Bouhassira D. Systemic lidocaine in pain due to peripheral nerve injury and predictors of response. *Neurology* 2004; 62:218-225.
60. Graff-Radford SB, Naliboff BD. Age predicts treatment outcome in postherpetic neuralgia. *Clinical Journal of Pain* 1988; 4:1-4.
61. van EF, Smits H, Geurts JW, Kessels AG, Kemler MA, van KM, Joosten EA, Faber CG. Brush-evoked allodynia predicts outcome of spinal cord stimulation in complex regional pain syndrome type 1. *EurJPain* 2010; 14:164-169.
62. van EF, Geurts J, van KM, Faber CG, Perez RS, Kessels AG, Van ZJ. Predictors of pain relieving response to sympathetic blockade in complex regional pain syndrome type 1. *Anesthesiology* 2012; 116:113-121.