J Rehabil Med 2019; 51: 183–192

ORIGINAL REPORT

PREDICTORS OF CHRONIC PAIN INTENSITY, SPREAD AND SENSITIVITY IN THE GENERAL POPULATION: A TWO-YEAR FOLLOW-UP STUDY FROM THE SWEPAIN COHORT

Britt LARSSON, PhD[1], Elena DRAGIOTI, PhD[1], Anna GRIMBY-EKMAN, PhD[2], Björn GERDLE, PhD[1] and Jonas BJÖRK, PhD[3]
From the [1]Pain and Rehabilitation Centre, and Department of Medical and Health Sciences, Linköping University, Linköping, [2]Health Metrics, University of Gothenburg, Gothenburg and [3]Division of Occupational and Environmental Medicine, Lund University, Lund, Sweden

Objective: **To determine whether the intensity, spread and sensitivity of chronic pain can be predicted using demographic features, socioeconomic conditions and comorbidities.**
Design: **A longitudinal study design was employed. Data was collected at baseline and at 2-year follow-up.**
Setting: **General population in south-eastern Sweden.**
Subjects: **A representative stratified random sample of 34,000 individuals, between 18 and 85 years of age, selected from a sampling frame of 404,661 individuals based on the Swedish Total Population Register.**
Methods: **Eligible individuals were sent postal surveys in 2013 and 2015. The 2 surveys included the same questions about basic demographic data, comorbidities, and chronic pain intensity, spread and sensitivity.**
Results: **Several socio-demographic features and comorbidities at baseline were significant predictors of characteristics of pain (intensity, spread and sensitivity) at the 2-year follow-up. When characteristics of pain at baseline were included in the regression analyses they were relatively strong significant predictors of characteristics of pain after 2 years. After this adjustment there were fewer socio-demographic and comorbidity predictors; the effect estimates for those significant predictors had decreased.**
Conclusion: **Clinical assessment should focus on several characteristics of pain and include a broad medical screening to capture the overall burden of pain in adults from a longitudinal perspective.**

Key words: general population; follow-up; chronic pain characteristics; sociodemographic; comorbidities.

Accepted Jan 3, 2019; Epub ahead of print Feb 27, 2019

J Rehabil Med 2019; 51: 183–192

Correspondence address: Britt Larsson, Pain and Rehabilitation Medicine, Department of Medical and Health Sciences (IMH), Faculty of Medicine and Health Sciences, Linköping University, SE-581 85 Linköping. E-mail: Britt.Larsson@liu.se

LAY ABSTRACT

This study shows how characteristics of chronic pain (intensity, spread and sensitivity) can be predicted using demographic and socioeconomic factors and other medical conditions. Information was collected from 34,000 individuals between 18 and 85 years of age in south-eastern Sweden. Several socio-demographic factors and other medical conditions were predictors of pain intensity, spread and sensitivity after 2 years. When pain characteristics were taken into consideration in the analysis they were relatively strong predictors of the pain characteristics after 2 years. After modification of the analysis, there were fewer socio-demographic and medical predictors and their importance had decreased. In planning treatment and rehabilitation for chronic pain, pain intensity, spread and sensitivity should specifically be taken into account.

Approximately 20% of the European population have moderate to severe chronic pain (CP) (>3 months) (1), hence it is important to elucidate the trajectory of CP and determine which factors affect this trajectory.

Longitudinal studies have investigated how CP itself, socio-demographic factors and comorbidities impact CP over time (2–8); however, the results of those studies often do not agree, and do not cover all important characteristics of pain. Some studies have predicted the presence of chronic widespread pain and/or spreading (of pain on the body) (2, 4–6). Other studies have predicted new onset of CP (3). Likewise, pain intensity (severity rated by the subject on a numeric scale) and pain sensitivity (increased pain responsiveness to noxious and/or non-noxious stimuli) are important aspects that contribute to the clinical presentation of CP (9, 10). Together with physical and emotional functions, comorbidities, coping strategies, and quality of life aspects, these characteristics of pain should be taken into account when elucidating the impact of pain (11–14).

Previous *cross-sectional epidemiological studies* have found that socio-demographic factors, such as age, sex, marital status, educational level and low income (15, 16), are associated with CP (i.e. duration >3 months).

Recent *longitudinal studies* have investigated the importance of some comorbidities, e.g. anxiety, depression, sleeping difficulties, body mass index (BMI) (2–6), or used an index for comorbidities (4). However, other comorbidities, e.g. heart disease, hypertension, diabetes and pulmonary disease, have also been as-

 doi: 10.2340/16501977-2519

sociated with CP (5, 17–19), and some of these are more frequent in widespread pain than in local pain (14). Moreover, some studies provide prediction models after adjustment for baseline pain (4, 5, 7), while others do not (6). Thus, it is not known whether the reported pattern of pain predictors would be the same if such adjustments were performed.

The impact of socioeconomic factors and comorbidities on characteristics of pain (intensity, spreading and sensitivity) might differ from the longitudinal perspective. More knowledge of predictors of intensity, spread and sensitivity of CP is needed, and it is reasonable to assume that several factors could serve as predictors for the development and persistence of different pain characteristics. There is agreement that both the pain experience and the CP condition must be bio-psychosocially assessed and managed in the clinical situation (20, 21).

The rationale for this study is that longitudinal associations between pain characteristics and sociodemographic and physical and psychological comorbidities have been incompletely examined in multivariate models.

The aim of this study was to elucidate the multivariate longitudinal associations, using 2-year follow-up epidemiological data (collected in 2013 and 2015) from a general population in south-eastern Sweden (the SWEPAIN cohort) to examine whether characteristics of pain are predicted by demographic features, socioeconomic conditions and certain comorbidities. It was hypothesized that:

- sociodemographic features and certain comorbidities would predict pain intensity, spread and sensitivity at a 2-year follow-up survey of a general population;
- baseline adjustments of pain intensity, spread of pain on the body, and sensitivity would markedly affect the pattern of important predictors.

METHODS

Design, subjects and procedures

The present study used data from the SWEPAIN cohort (14, 22), which has been approved by the local ethics committee of Linköping University, Sweden (Dnr: 2011 72/31). Baseline data (T0) were collected using a stratified random sample of 34,000 individuals from a sampling frame based on the Swedish Total Population Register. The sample frame consisted of 404,661 individuals who were 16–85 years old and living in south-eastern Sweden.

The random sampling was stratified by sex and municipality to reach individuals living in urban and rural areas (14). Data were collected by Statistics Sweden. The selected individuals received a postal questionnaire in March 2013, which could be returned either by post or electronically. A reminder was sent to non-responders after 2 weeks and, if necessary, another reminder was sent 2 weeks later. The collection of questionnaires ended in May 2013. Follow-up data (T1) were collected 2 years later. Only individuals who completed and returned the first questionnaire were eligible to participate in the follow-up assessment. Eligible individuals received a postal survey in March 2015, which could be returned by post or electronically. Two reminders were sent. Collection of follow-up data ended in May 2015. The surveys at T0 and T1 included the same questions. The Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) (23) statement was followed.

Predictor variables

Sociodemographic features. The survey questions about basic demographic data (age and sex), country of birth (Sweden vs abroad (i.e. being an immigrant)), citizenship (Swedish vs other), marital status (single, married, divorced, or widowed), educational level (elementary school, secondary upper school/vocational training, or university education), employment status (employment vs unemployment), and household annual income in 2010.

Physical and psychological comorbidities. Assessment of comorbidities was based on a self-reported questionnaire published elsewhere (10, 24, 25). A copy of the questionnaire is available from the corresponding author on request. Briefly, it covers 12 disorders and diseases: traumatic injuries; rheumatoid arthritis and osteoarthritis (RA/OA); cardiovascular disorders (CVD, including high blood pressure, angina pectoris, and heart attacks); pulmonary disorders; gastrointestinal (GI) disorders; disorders of the central nervous system (CNS) (including ophthalmological and ear–nose–throat disorders); urogenital disorders; skin disorders; tumours and cancer; metabolic diseases (including diabetes, obesity, anorexia, bulimia, and goitre); depression; and anxiety. These comorbidities were reported on a 5-point scale: 1: no; 2: yes, according to both my own and my doctor's opinions; 3: yes, according to my own opinion; 4: yes, according to my doctor's opinion; and 5: I do not know. The answers for 2, 3, and 4 were combined into category "yes" in order to obtain a robust measurement of the presence of the specific comorbidity vs the answer "no" (10, 24, 25). The answer option "I do not know" was also recorded as "no". Self-reported assessments of comorbidities are widely used in the literature and have been reported to be reliable (26).

Selection of predictor variables

The selection of these predictor variables (e.g. socio-demographic factors and comorbidities) was based on recognized associations with pain intensity, spread and sensitivity of pain (2–8, 27–31) and on disease states common worldwide.

Outcome variables

Definition of chronic pain. All respondents were asked to report if they had CP, defined by a single question "Do you frequently (usually) have pain lasting more than 3 months?" (yes/no). Subjects who responded "no" were assigned to the no pain (NP) cohort, while those who responded "yes" were assigned to the chronic pain (CP) cohort.

Pain intensity. Only those respondents who were assigned to the CP cohort were additionally asked to complete their mean pain intensity during the previous 7 days on a numeric rating scale (NRS7d) (0=not at all to 10=worst imaginable pain) (32).

Pain spreading categories based on the number and location of pain sites. The participants with pain marked the site of their pain during the previous 7 days on a body chart divided into 45 sections (22 on the front and 23 on the back) (14). One marked

area corresponds to 1 pain site; hence, the maximum number of pain sites was 45. Based on these 45 pain sites, 23 anatomical regions were determined and a total pain index, ranging from 0 to 23, was considered (22). Using a slightly modified definition developed by MacFarlane et al. (33), widespread pain (WSP) was defined as pain in at least 2 sections in 2 contralateral limbs and the axial skeleton and marked equally on the front and back of the chart. MacFarlane et al. defined WSP in the limbs to be present "if there are at least 2 painful sections (in 2 contralateral limbs)", a definition that does not require pain to be marked equally on the front and back of the chart (33). Therefore, the current study uses a stricter definition of WSP than the American College of Rheumatology criteria (34). In addition to WSP, the following categories were defined: 1: No pain (NP) if the participants reported zero anatomical sites with pain (i.e. pain index = 0) and answered "no" to the question "Do you frequently ('usually') have pain lasting more than 3 months?" and did not report on pain intensity above (this group served as the reference; category = 0); 2: Local pain (LP) if the participants reported 1–2 anatomical sites; 3: Regional Pain-Medium (RP-Medium) if the participants reported 3–6 anatomical sites with pain; and 4: Regional Pain-Heavy (RP-Heavy) if the participants reported 7–17 anatomical pain sites with pain, but which did not fulfil the WSP criteria. WSP, a common clinical entity, depends both on the number of pain sites and their spatial distribution. As discussed elsewhere (14), a minority of subjects with RP-Heavy could have a higher number of pain sites than some of the subjects with WSP (14); however, in this study the 95% confidence intervals (95% CI) for the number of pain sites clearly differed between RP-Heavy and WSP (Table SI[1]).

Pain sensitivity. Pain sensitivity was assessed by all participants using the Pain Sensitivity Questionnaire (PSQ), which consists of 17 items that each describe a daily life situation (35). The PSQ asks all participants to rate how intense pain in each situation would be for them on an NRS (ranging from 0 = not painful at all to 10 = worst pain imaginable). Whereas 14 of the items relate to situations that are assessed as painful by a majority of healthy subjects, 3 items describe situations that are usually not rated as painful (e.g. taking a warm shower). These 3 items are interspersed between the items to serve as non-painful sensory reference for the individuals and were not considered when calculating the final score. The items cover a range of pain intensities, a variety of pain types (e.g. hot, cold, sharp, and blunt), and body sites (head, upper extremity, and lower extremity). The mean of the 14 items mentioned above (relate to situations that are assessed as painful by most healthy subjects) was calculated (range 0–10). In this study, we used the Swedish adaptation of the PSQ (22). The Cronbach's alpha was 0.93 (22). However, the Swedish version of the PSQ has so far not been validated. Since reliability, content, structural validity, and hypothesis testing regarding (36) the PSQ were quite consistently good across 3 investigated languages and cultures (35, 37, 38), there is good reason to believe the same for the Swedish version.

Data analysis

All statistical analyses were performed using IBM SPSS Statistics (version 23.0; IBM Inc., New York, USA). The sampling weights for unequal possibilities of sample selection have been reported elsewhere (14) Two-sided statistical tests were used and $p < 0.05$ was regarded as significant. Distributions and descriptive statistics were examined for all variables for the total sample at T0 and T1. Means and standard deviations (SDs) were calculated for continuous variables, and frequencies with percentages (*n*; %) were calculated for categorical variables.

The prospective 2-year follow-up analysis of each pain outcome (i.e. pain intensity, spread and sensitivity) was performed through a series of generalized linear models (GLM) used as prediction models with baseline variables as predictors. GLM is a flexible generalization of ordinary linear regression analyses that allow for response variables that have error distribution models other than a normal distribution (39). In the case of pain intensity and pain sensitivity, which served as linear-response data, the identity link function was used with maximum likelihood estimation (MLE) and results are presented as parameter estimates (B) with Wald 95% CIs. In the case of the outcome of the pain spreading categories, which served as an ordinal response variable, the ordinal logit function was used, yielding odds ratios (OR) and Wald 95% CIs. The significance of the estimated effects in all GLM analyses was evaluated using the Wald test (39). For analytical purposes in the prediction models, the categorical variables were dichotomized and entered as follows: sex (female = 1), country of birth (abroad = 1) citizenship (other = 1), marital status (married = 1), educational level (university, i.e. higher education=1), employment status (unemployment = 1), and existence of a certain comorbidity (yes = 1).

To determine the variables to include in the multivariable model, separate univariable analyses were performed with each independent variable 1 at a time (single predictor model). Only variables with $p < 0.20$ in the single model were included in the multivariable model. Next, we examined for multicollinearity between the significant independent variables as derived by univariable analyses by performing linear regression and by examining tolerance and the variance inflation factor (VIF). A tolerance of less than 0.20 or 0.10 and/or a VIF of 5 or 10 and above indicates a multicollinearity problem (40). In the case of multicollinearity, we also performed Pearson correlation (r) analysis to test for bivariate correlations between the continuous variables and phi coefficient (41), a measure of association between the binary variables. High bivariate correlation coefficients ≤ 0.7 or phi (Φ) ≤ 0.3 (39, 40) indicate risk of collinearity; in that case, only 1 of the 2 highly correlated variables were included. Hence, citizenship as well as anxiety were excluded from all multivariable models due to high correlation with birth country ($\Phi = 0.45$) and depression ($\Phi = 0.70$), respectively. After exclusion of the above variables, tolerance and variance inflation revealed that there was no serious indication of multicollinearity. Birth country and depression were kept in the model as they exhibited more pronounced parameter estimates in univariable analysis than citizenship and anxiety.

Two multivariable prediction models are presented. In model 1, all selected baseline (T0) variables according to the *p*-value criteria of $p < 0.20$ with respect to the single predictor model (with exception of highly correlated variables) were included in 1 multivariable model. In model 2, all variables from the multivariable model 1 along with the 3 pain characteristics for each outcome of interest were simultaneously controlled for. Hence, pain intensity, spread of pain and sensitivity at T0 were entered in the multivariable model 2, and only complete cases were included. These 2 models address different, but interrelated questions: 1: Which socio-demographic features and comorbidities at baseline (T0) predict pain at follow-up (T1)? And: 2: How do these predictive associations change when differences in pain present already at baseline are adjusted for? Model 1 thus provides estimates of cumulative associations with pain, whereas the adjustment for pain at baseline in model 2 implies that associations with changes in pain occurring during follow-up are estimated.

[1]http://www.medicaljournals.se/jrm/content/?doi=10.2340/16501977-2519

In all prediction models, the spread of pain variable was used as a continuous variable (referred to as being covariate) when adjusting for spread of pain at T0. A subsequent sensitivity analysis was also performed, treating spread of pain at T0 as an ordinal covariate. At the follow-up, approximately 13–31% of the observations were missing. Regarding pain intensity, missing cases were calculated based on valid responses instead of the total sample, since pain-free respondents did not answer this question.

Response rate and drop-out analysis for T0 and at 2-year follow-up (T1)

At baseline (T0), 15,781 individuals (54% female) completed and returned the questionnaire, a response rate of 46.4%. Another 218 subjects were excluded due to missing values to vital questions (e.g. pain characteristics) of the survey. Hence, the final response rate at T0 was 45.8%. Of the 15,563 respondents, 56.8% were in the non-pain cohort (NP) and 43.2% in the CP cohort. The response rate at T0 was lower among men, single people and immigrants (Table I).

At the 2-year follow-up survey (T1), 11,386 individuals (55% female) completed and returned the questionnaire, which constituted a total of 73% rate of the 15,563 individuals who responded to the first survey in 2013; 54.5% were in NP, and 45.5% in the CP cohort. The response rate at T1 was lower among younger ages, men, single people, secondary educated, unemployed, not Swedish, lower household income, depression and anxiety (Table I).

RESULTS

Descriptive statistics at 2-year follow-up (T1)

Age range at the 2-year follow-up (T1) was 18–87 years (mean age 55.8; SD 17.5 years) and 55% were female. Additional sociodemographic features at T1

Table I. Sociodemographic characteristics and study measures at baseline (T0), and at 2-year follow-up (T1), and characteristics of non-participants at both times

	Baseline (T0)		Follow-up (T1)		Baseline (T0)	Follow-up (T1)
Characteristics	Number of answers	Participants (n = 15,563)	Number of answers	Participants (n = 11,386)	Non-participants (n = 18,219)	Non-participants (n = 4,177)
Age, years, mean (SD)	15,563	51.6 (18.5)	11,384	55.8 (17.5)	–	45.6 (19.5)
Sex, *n* (%)	15,563		11,386			
Male		7,151 (46.0)		5,125 (45.0)	9,837 (54.0)	2,026 (48.5)
Female		8,412 (54.0)		6,261 (55.0)	8,382 (46.0)	2,151 (51.5)
Marital status, *n* (%)	15,555		11,386			
Single		5,134 (33.0)		3,179 (27.9)	9,440 (51.8)	1,851 (44.3)
Married		7,825 (50.3)		6,105 (53.6)	6,347 (34.8)	1,721 (41.2)
Divorced		1,762 (11.3)		1,387 (12.2)	1,802 (9.9)	411 (9.8)
Widowed		834 (5.4)		715 (6.3)	630 (3.5)	191 (4.6)
Educational level, *n* (%)	15,256		11,162			
Elementary school		3,442 (22.6)		2,491 (22.3)	–	871 (21.5)
Secondary school or vocational training		6,225 (40.8)		4,257 (38.2)	–	1,898 (46.9)
College or university		5,589 (36.6)		4,414 (39.5)	–	1,282 (31.6)
Employment status, *n* (%)	15,115		11,002			
Employment		8,708 (57.6)		6,213 (56.5)	–	2,342 (58.4)
Unemployment		6,407 (42.4)		4,789 (43.5)	–	1,671 (51.6)
Country of birth, *n* (%)	15,563		11,386			
Sweden		14,093 (90.6)		10,496 (92.2)	14,475 (79.5)	3,597 (86.1)
Abroad (i.e. immigrant)		1,470 (9.4)		890 (7.8)	3,744 (20.5)	580 (13.9)
Citizenship, *n* (%)	15,563		11,386			
Swede		15,197 (97.7)		11,194 (98.3)	16,786 (92.1)	4,019 (96.2)
Other		366 (2.3)		192 (1.7)	1,433 (7.9)	158 (3.8)
Household income, Euros per year, mean (SD)	15,510	55,270 (35,157)	11,386	58,419 (35,919)	–	51,834 (36014)
Pain intensity (NRS7d), mean (SD)	6,870	4.8 (2.0)	5,305	4.7 (2.0)	–	4.9 (2.1)
Pain spreading, *n* (%)	15,562		11,386			
NP		8,851 (56.9)		6,201 (54.5)	–	2,364 (56.6)
LP		2,580 (16.6)		2,046 (18.0)	–	690 (16.5)
RPM		2,989 (19.2)		2,359 (20.7)	–	781 (18.7)
RPH		823 (5.3)		559 (4.9)	–	247 (5.9)
WSP		319 (2.0)		221 (1.9)	–	95 (2.3)
Pain sensitivity (mean PSQ), mean (SD)	15,415	3.7 (1.5)	11,278	3.9 (1.5)	–	3.8 (1.6)
Comorbidities, *n* (%)						
Traumatic injuries	14,887	1,506 (10.1)	10,800	1,013 (9.4)	–	436 (11.2)
Rheumatoid arthritis–osteoarthritis (RA/OA)	14,932	2,823 (18.9)	10,595	2,307 (21.8)	–	629 (16.5)
Cardiovascular disorders (CVD)	14,901	3,295 (22.1)	10,766	2,719 (25.3)	–	700 (18.1)
Pulmonary disorders	14,972	1,614 (10.8)	10,816	1,169 (10.8)	–	488 (12.5)
Gastrointestinal disorders (GI)	15,012	2,453 (16.3)	10,752	1,793 (16.7)	–	680 (17.6)
Disorders of the CNS	15,001	2,993 (20.0)	10,865	2,218 (20.4)	–	754 (19.3)
Urogenital disorders	14,883	725 (4.9)	10,740	582 (5.4)	–	200 (5.2)
Skin disorders	14,968	1,851 (12.4)	10,861	1,356 (12.5)	–	511 (13.1)
Tumours/cancer	14,687	545 (3.7)	10,635	454 (4.3)	–	160 (4.2)
Metabolic disorders	15,000	1,559 (10.4)	10,852	1,223 (11.3)	–	400 (10.3)
Depression	14,878	2,092 (14.1)	10,598	1,513 (14.3)	–	666 (17.7)
Anxiety	14,868	2,537 (17.1)	10,570	1,842 (17.4)	–	830 (21.9)

PSQ: Pain Sensitivity Questionnaire; SD: standard deviation; CNS: central nervous system; NP: no pain, LP: local pain; RPM: Regional Pain-Medium; RPH: Regional Pain-Heavy; WSP: widespread pain, N: total number of participants.

are reported in Table I. The mean pain intensity for responders with pain at T1 was 4.7 (SD 2.0) and the mean pain sensitivity (PSQ) was 3.9 (SD 1.5) among all respondents at T1. The prevalence of NP was 54.5%. Of all the respondents at T1, the prevalence of LP was 18.0%, RP-Medium 20.7%, RP-Heavy 4.9%, and WSP 1.9%.

Table I also reports physical and psychological comorbidities. The most common comorbidities at T1 were as follows: CVDs (25.3%), RA/OA (21.8%), and CNS disorders (20.4%).

Predicting pain intensity at T1

The univariable and multivariable analyses are presented in Table II. Univariable analyses showed that all the examined variables at T0, except citizenship, had *p*-values below 0.05 in their associations with pain intensity at T1. In the multivariable analysis, without any pain characteristics at T0 included, female sex, immigrant, traumatic injuries, RA/OA, CVDs, pulmonary, GI, CNS and metabolic disorders, and depression at T0 were positive predictors of pain intensity at T1, whereas age and higher education were protective predictors (Table II; multivariable model 1).

When the 3 investigated characteristics of pain at T0 were introduced as predictors, they were all positive predictors (Table II; multivariable model 2). Female sex, traumatic injuries, CVDs, and pulmonary disorders remained as positive predictors. Only high education remained as a protective predictor (Table II; multivariable model 2).

Predicting spread of pain at T1

The univariable and multivariable analyses are presented in Table III. Univariable analysis showed that all the examined variables at T0, except for citizenship, were clearly associated with spread of pain at T1 ($p < 0.001$). Multivariate analysis, without any pain characteristics at T0, showed that being female, immigrant, all studied comorbidities except for pulmonary and urogenital disorders, and tumours/cancer were positive significant predictors of spread of pain at T1, whereas higher education and unemployment were significant protective predictors (Table III; multivariable model 1).

When the 3 pain characteristics at T0 were introduced as predictors, the following variables remained as positive predictors: female, traumatic injuries, RA/OA, CNS, and GI disorders, whereas higher education and unemployment disappeared as predictors (Table III; model 2). In addition, all pain characteristics at T0 were positive predictors for spread of pain at T1 (Table III; multivariable model 2).

Table II. Baseline predictors (T0) for pain intensity at 2-year follow-up (T1)

	Univariable			Multivariable 1 (N = 4,473; 15.7% missing data)*			Multivariable 2 (N = 3,823; 28.1% missing data)*		
Baseline predictors	Estimate (B)	95% CI	*p*-value	Estimate (B)	95% CI	*p*-value	Estimate (B)	95% CI	*p*-value
Pain intensity	0.51	0.48, 0.54	**<0.001**	–	–	–	0.43	0.40, 0.47	**<0.001**
Pain spreading[a]	0.52	0.47, 0.56	**<0.001**	–	–	–	0.13	0.06, 0.20	**<0.001**
Pain sensitivity	0.27	0.24, 0.31	**<0.001**	–	–	–	0.08	0.04, 0.11	**<0.001**
Age, years	0.10	0.05, 0.15	**<0.001**	−0.13	−0.21, −0.06	**0.001**	−0.03	−0.11, 0.05	0.501
Sex (female/male[b])	0.35	0.24, 0.46	**<0.001**	0.34	0.23, 0.46	**<0.001**	0.14	0.03, 0.26	**0.019**
Marital status (married/other[b])	0.14	0.07, 0.20	**<0.001**	0.08	0.00, 0.16	0.052	0.06	−0.02, 0.13	0.163
Educational level (university/other[b])	−0.35	−0.41, −0.28	**<0.001**	−0.29	−0.37, −0.21	**<0.001**	−0.13	−0.22, −0.05	**0.001**
Employment (unemployed/employed[b])	0.35	0.25, 0.46	**<0.001**	0.03	−0.11, 0.16	0.712	0.02	−0.12, 0.16	0.765
Country of birth (abroad/Sweden[b])	0.59	0.41, 0.77	**<0.001**	0.31	0.12, 0.51	**0.002**	0.05	−0.16, 0.28	0.739
Citizenship (other/Sweden[b])	0.38	−0.03, 0.78	0.070	–	–	–	–	–	–
Household income, Euros per year	−0.18	−0.22, −0.13	**<0.001**	−0.03	−0.08, 0.03	0.322	−0.04	−0.09, 0.02	0.166
Traumatic injuries (yes/no[b])	0.65	0.50, 0.79	**<0.001**	0.45	0.30, 0.60	**<0.001**	0.25	0.10, 0.39	**0.001**
Rheumatoid arthritis-osteoarthritis (yes/no[b])	0.69	0.58, 0.81	**<0.001**	0.45	0.32, 0.57	**<0.001**	0.11	−0.01, 0.24	0.077
Cardiovascular disorders (yes/no[b])	0.47	0.35, 0.59	**<0.001**	0.31	0.17, 0.44	**<0.001**	0.21	0.07, 0.35	**0.002**
Pulmonary disorders (yes/no[b])	0.65	0.49, 0.81	**<0.001**	0.32	0.15, 0.49	**<0.001**	0.22	0.05, 0.38	**0.011**
Gastrointestinal disorders (yes/no[b])	0.55	0.42, 0.67	**<0.001**	0.29	0.15, 0.42	**<0.001**	0.12	−0.02, 0.25	0.091
Disorders of the CNS (yes/no[b])	0.40	0.28, 0.52	**<0.001**	0.17	0.04, 0.30	**0.012**	−0.02	−0.15, 0.10	0.716
Urogenital disorders (yes/no[b])	0.58	0.36, 0.80	**<0.001**	0.23	−0.01, 0.47	0.061	0.05	−0.19, 0.28	0.696
Skin diseases (yes/no[b])	0.25	0.10, 0.41	**0.001**	0.03	−0.13, 0.19	0.694	0.01	−0.15, 0.17	0.891
Tumours/cancer (yes/no[b])	0.28	0.01, 0.54	**0.041**	0.03	−0.27, 0.32	0.851	0.14	−0.17, 0.45	0.364
Metabolic disorders (yes/no[b])	0.55	0.39, 0.70	**<0.001**	0.23	0.07, 0.40	**0.006**	0.03	−0.13, 0.19	0.297
Depression (yes/no[b])	0.57	0.43, 0.70	**<0.001**	0.31	0.16, 0.45	**<0.001**	0.13	−0.02, 0.27	0.082
Anxiety (yes/no[b])	0.46	0.33, 0.59	**<0.001**	–	–	–	–	–	–

*N = number of complete cases included in the models out of a total of 5,305 valid responses for pain intensity. Pain intensity was measured only in pain population. [a]Baseline spread of pain was entered to the models as covariate with 5 levels 0 = no pain, 1 = local pain, 2 = Regional Pain-Medium, 3 = Regional Pain-Heavy, and 4 = widespread pain. [b]Reference category.
CNS: central nervous system; B: unstandardized regression coefficient; CI: Wald confidence interval; multivariable 1: all baseline variables together in 1 model without baseline pain dimensions; Multivariable 2: all baseline variables from multivariable model 1, including baseline pain dimensions. Significant differences in bold.

Table III. Baseline predictors (T0) for pain spreading (NP, LP, RP-Medium, RP-Heavy, and WSP) at 2-year follow-up (T1) treated as an ordinal outcome

	Univariable			Multivariable 1 (n = 8,860; 22.2% missing data)*			Multivariable 2 (n = 7,874; 30.8% missing data)*		
Baseline predictors	Estimate (OR)	95% CI	p-value	Estimate (OR)	95% CI	p-value	Estimate (OR)	95% CI	p-value
Pain intensity	1.31	1.27, 1.34	**<0.001**	–	–	–	1.15	1.11, 1.19	**<0.001**
Pain spreading[a]	4.09	3.92, 4.27	**<0.001**	–	–	–	2.93	2.69, 3.18	**<0.001**
Pain sensitivity	1.21	1.17, 1.24	**<0.001**	–	–	–	1.04	1.01, 1.08	**0.041**
Age, years	1.15	1.12, 1.19	**<0.001**	0.95	0.90, 1.01	0.065	0.99	0.92, 1.08	0.944
Sex (female/male[b])	1.77	1.65, 1.90	**<0.001**	1.70	1.56, 1.84	**<0.001**	1.46	1.30, 1.65	**<0.001**
Marital status (married/other[b])	1.18	1.12, 1.23	**<0.001**	1.00	0.94, 1.06	0.976	0.93	0.86, 1.02	0.099
Educational level (university/other[b])	0.80	0.77, 0.84	**<0.001**	0.86	0.84, 0.94	**<0.001**	0.98	0.90, 1.06	0.979
Employment (unemployed/employed[b])	1.24	1.15, 1.33	**<0.001**	0.76	0.69, 0.84	**<0.001**	0.94	0.81, 1.08	0.402
Country of birth (abroad/Sweden[b])	1.47	1.29, 1.67	**<0.001**	1.33	1.15, 1.55	**<0.001**	0.95	0.77, 1.18	0.952
Citizenship (other/Sweden[b])	0.96	0.74, 1.26	0.785	–	–	–	–	–	–
Household income, Euros per year	0.87	0.84, 0.89	**<0.001**	0.97	0.94, 1.01	0.165	0.97	0.91, 1.02	0.966
Traumatic injuries (yes/no[b])	3.53	3.15, 3.96	**<0.001**	2.74	2.41, 3.12	**<0.001**	1.59	1.36, 1.85	**<0.001**
Rheumatoid arthritis/osteoarthritis (yes/no[b])	4.26	3.90, 4.65	**<0.001**	3.49	3.14, 3.86	**<0.001**	1.50	1.31, 1.71	**<0.001**
Cardiovascular disorders	1.55	1.43, 1.68	**<0.001**	1.21	1.09, 1.35	**<0.001**	0.94	0.82, 1.08	0.401
Pulmonary disorders (yes/no[b])	1.76	1.57, 1.97	**<0.001**	1.13	0.98, 1.27	0.084	1.02	0.86, 1.22	0.807
Gastrointestinal disorders (yes/no[b])	2.71	2.46, 2.98	**<0.001**	1.85	1.66, 2.05	**<0.001**	1.40	1.21, 1.61	**<0.001**
Disorders of the CNS (yes/no[b])	2.11	1.94, 2.30	**<0.001**	1.54	1.39, 1.71	**<0.001**	1.14	1.00, 1.31	**0.048**
Urogenital disorders (yes/no[b])	1.83	1.55, 2.14	**<0.001**	1.19	0.98, 1.45	0.075	1.05	0.81, 1.34	0.735
Skin diseases (yes/no[b])	1.57	1.41, 1.74	**<0.001**	1.23	1.09, 1.38	**<0.001**	1.12	0.95, 1.32	0.186
Tumours/cancer (yes/no[b])	1.42	1.18, 1.71	**<0.001**	0.93	0.73, 1.17	0.533	0.91	0.66, 1.25	0.910
Metabolic disorders (yes/no[b])	1.92	1.72, 2.15	**<0.001**	1.31	1.15, 1.49	**<0.001**	1.13	0.95, 1.34	0.169
Depression (yes/no[b])	2.54	2.29, 2.82	**<0.001**	1.82	1.62, 2.05	**<0.001**	1.15	0.98, 1.34	0.081
Anxiety (yes/no[b])	2.28	2.07, 2.51	**<0.001**	–	–	–	–	–	–

*n = number of complete cases included in the models out of a total of 11,386 respondents. [a]Baseline spread of pain was entered to the models as covariate with 5 levels 0=no pain, 1=local pain, 2=Regional Pain-Medium, 3=Regional Pain-Heavy, and 4=widespread pain. [b]Reference category.
OR: Odds ratio; CI: Wald confidence interval; NP: No pain; LP: Local pain; RP-Medium: Regional pain medium; RP-Heavy: Regional pain heavy; WSP: widespread pain; CNS: central nervous system; Multivariable 1: all baseline variables together in 1 model without baseline pain dimensions; Multivariable 2: all baseline variables from multivariable model 1, including baseline pain dimensions. Significant differences in bold.

Predicting pain sensitivity at T1

The univariable and multivariable analyses are presented in Table IV. The univariate analysis showed that all the examined variables at T0, except for traumatic injuries, had p-values below 0.05 in their associations with pain sensitivity at T1 (all $p < 0.05$). In the multivariable analysis without the pain, characteristics at T0 included female, immigrant, RA/OA, pulmonary, GI, urogenital, and metabolic disorders, and were positive significant predictors (Table IV; multivariable model 1).

When the 3 pain characteristics at T0 were introduced as predictors, only pain sensitivity at T0 was a positive significant predictor of pain sensitivity at T1 (Table IV; multivariable model 2). Only immigrant and metabolic disorders remained as positive significant predictors. The results of the current study regarding all 3 outcome variables remained to a great degree when the spread of pain at T0 was used as an ordinal covariate in a subsequent sensitivity analysis (Table SII[1]).

DISCUSSION

Several socio-demographic features and comorbidities at T0 were significant predictors of pain intensity, spread and sensitivity 2 years later (T1). When the pain characteristics at T0 (i.e. intensity, spread and sensitivity) were included, these were relatively strong significant predictors of intensity and spread at T1. After that adjustment, both socio-demographic and comorbidity predictors were substantially fewer and for those significant predictors their effect estimates had generally decreased. It is notable that being female and traumatic injuries were likewise significant predictors, together with the 3 pain characteristics, for pain intensity and spread at T1; unique predictors (education level and being an immigrant) also existed for these 2 pain characteristics. Pain sensitivity was the only characteristic of pain at T0, and being an immigrant and metabolic disorders that significantly predicted sensitivity at T1.

It should be stressed that the inclusion of pain characteristics at baseline changes the interpretation of the model from a prediction of pain at T1 (multivariable model 1) to a prediction of the change in pain at T1 (multivariable model 2). The results indicate that socioeconomic factors and comorbidities were more common and stronger risk factors for the cumulative burden of pain than for changes during the medium- to short-term. The results also indicate that current pain intensity, anatomical spread, and sensitivity strongly influence the course of CP intensity and spread. The impact of single pain characteristics on the burden of pain over time has been reported previously. For example,

Table IV. Baseline predictors (T0) for pain sensitivity (Pain Sensitivity Questionnaire (PSQ)) at 2-year follow-up (T1)

	Univariable			Multivariable 1 (N=9,880; 13.3% missing data) *			Multivariable 2 (N=8,873; 22.1% missing data) *		
Baseline predictors	Estimate (B)	95% CI	*p*-value	Estimate (B)	95% CI	*p*-value	Estimate (B)	95% CI	*p*-value
Pain intensity	0.16	0.14, 0.18	**<0.001**	–	–	–	–0.02	–0.03, 0.02	0.089
Pain spreading[a]	0.21	0.19, 0.24	**<0.001**	–	–	–	0.02	–0.02, 0.06	0.391
Pain sensitivity	0.72	0.70, 0.73	**<0.001**	–	–	–	0.72	0.69, 0.74	**<0.001**
Age, years	0.05	0.02, 0.07	**<0.001**	–0.03	–0.07, 0.03	0.074	0.03	–0.04, 0.09	0.420
Sex (female/male[b])	0.16	0.10, 0.21	**<0.001**	0.11	0.06, 0.17	**<0.001**	0.02	–0.03, 0.06	0.484
Marital status (married/other[b])	0.05	0.02, 0.08	**<0.001**	0.01	–0.04, 0.05	0.807	0.03	–0.02, 0.08	0.310
Educational level (university/other[b])	–0.17	–0.21, –0.14	**<0.001**	–0.14	–0.18, –0.10	**<0.001**	–0.01	–0.06, 0.04	0.714
Employment (unemployed/employed[b])	0.19	0.14, 0.27	**<0.001**	0.03	–0.03, 0.10	0.330	0.05	–0.03, 0.13	0.246
Country of birth (abroad/Sweden[b])	0.79	0.69, 0.89	**<0.001**	0.64	0.53, 0.75	**<0.001**	0.28	0.16, 0.40	**<0.001**
Citizenship (other/Sweden[b])	0.52	0.32, 0.72	**<0.001**	–	–	–	–	–	–
Household income, Euros per year	–0.11	–0.13, –0.08	**<0.001**	–0.03	–0.05, 0.01	0.070	–0.01	–0.04, 0.02	0.486
Traumatic injuries (yes/no[b])	0.06	–0.03, 0.15	0.217	–	–	–	–	–	–
Rheumatoid arthritis/osteoarthritis (yes/no[b])	0.31	0.24, 0.37	**<0.001**	0.14	0.07, 0.22	**<0.001**	–0.02	–0.09, 0.05	0.518
Cardiovascular disorders (yes/no[b])	0.18	0.12, 0.4	**<0.001**	0.03	–0.04, 0.11	0.373	–0.02	–0.09, 0.06	0.665
Pulmonary disorders (yes/no[b])	0.16	0.07, 0.25	**<0.001**	–0.03	–0.12, 0.07	0.654	–0.03	–0.12, 0.07	0.662
Gastrointestinal disorders (yes/no[b])	0.27	0.20, 0.35	**<0.001**	0.13	0.05, 0.21	**0.001**	0.03	–0.06, 0.11	0.506
Disorders of the CNS (yes/no[b])	0.20	0.13, 0.26	**<0.001**	0.07	–0.01, 0.14	0.062	–0.01	–0.08, 0.07	0.936
Urogenital disorders (yes/no[b])	0.35	0.22, 0.47	**<0.001**	0.16	0.02, 0.30	**0.025**	–0.06	–0.19, 0.08	0.419
Skin diseases (yes/no[b])	0.10	0.02, 0.18	**0.014**	0.04	–0.05, 0.13	0.358	0.02	–0.08, 0.11	0.724
Tumours/cancer (yes/no[b])	0.24	0.09, 0.38	**0.002**	0.09	–0.07, 0.26	0.188	0.17	–0.01, 0.34	0.067
Metabolic disorders (yes/no[b])	0.36	0.27, 0.45	**<0.001**	0.25	0.15, 0.35	**<0.001**	0.13	0.03, 0.22	**0.014**
Depression (yes/no[b])	0.41	0.32, 0.48	**<0.001**	0.25	0.16, 0.33	**<0.001**	–0.02	–0.12, 0.08	0.662
Anxiety (yes/no[b])	0.41	0.34, 0.49	**<0.001**	–	–	–	–	–	–

*N = number of complete cases included in the models out of a total of 11,386 respondents. [a]Baseline spread of pain was entered to the models as covariate with 5 levels 0 = no pain, 1 = local pain, 2 = Regional Pain-Medium, 3 = Regional Pain-Heavy, and 4 = widespread pain. [b]Reference category.
B: unstandardized regression coefficient; CI: Wald confidence interval; CNS: central nervous system. Multivariable 1: all baseline variables together in 1 model without baseline pain dimensions; Multivariable 2: all baseline variables from multivariable model 1, including baseline pain dimensions. Significant differences in bold.

pain intensity has been shown to predict increased pain intensity (31, 42) and to predict CP (single characteristics of pain not presented) (43). Spread of pain was associated with CP (single characteristics of pain not presented) at follow-up (44, 45) and anatomical spread of pain at follow-up (46, 47). In non-longitudinal studies, spread of pain has been found to be significantly correlated with pain intensity (48, 49). In a systematic review, both pain spread and intensity were considered prognostic factors for CP (single pain characteristics not presented) (50). The multivariable models 2 in the current study provides a comprehensive overview on the impact of 3 characteristics of pain (intensity, spread and sensitivity) on the burden of pain over time. Based on the results of the present study and the above studies, future longitudinal studies should investigate risk factors for several characteristics of pain and include these characteristics of pain at baseline in order to predict accurately how pain develops.

Other longitudinal studies that tried to detect significant predictors in relation to CP thus restricted their analysis mostly to 1 characteristic of pain or to a general label of pain. As argued in the introduction, such a unidimensional approach is from a clinical point of view a too simplistic description of pain *per se*. To the best of our knowledge, this study is the first comprehensive attempt to ascertain predictors of different common clinical characteristics of CP in the light of the concept and perception of pain as a multifaceted phenomenon. The results of the current study highlight that the features of the predictors in the final models are only to a limited extent common for the 3 characteristics of pain investigated. Furthermore, this study suggests that CP, as most often defined and as defined in this study, constitutes a general indicator for several clinical characteristics of CP. It appears that characteristics of pain, such as intensity, anatomical spread, and sensitivity, only partly reflect similar underlying neurobiological mechanisms both in the cross-sectional and longitudinal perspectives. Hence, recent cross-sectional studies of muscle and plasma in patients with CP conditions have shown that pain intensity and pain sensitivity (i.e. pressure pain thresholds) are associated with different molecular mechanisms from a protein pattern perspective (51, 52). Moreover, the characteristics of pain investigated may be, at least partly, processed differently in the CNS and have different associations with other conditions, such as psychological symptoms.

The current longitudinal results confirm the results of previous (mostly cross-sectional) studies, suggesting associations between sociodemographic factors and single characteristics of pain (1, 15, 16, 53–55) and that such factors are less predictive of short- to medium-term changes in pain.

The present longitudinal study found being female to be a predictor for pain intensity (Table II, multivariable

model 1), spread (Table III, multivariable model 1) and sensitivity (Table IV, multivariable model 1). In addition, being female was still a predictor of intensity and spread of pain when pain variables at baseline were included as regressors (Tables II, III, multivariable model 2).

Low education level was a predictor for an increase in the 3 characteristics of pain (Tables II–IV multivariable models 1) and a predictor of pain intensity in multivariable model 2. In cross-sectional studies, low education has been related to CP intensity (56–58) and spread (2, 5, 31, 59). These associations may reflect physical exposures in working life that are more common among individuals with low education, which contribute to the development of CP (60).

Being an immigrant was a predictor of the 3 characteristics of pain (Tables II–IV, multivariable models 1) and a predictor of pain sensitivity when pain variables were included as predictors (Table IV, multivariable model 2). Being an immigrant has been related to spread of CP (61, 62) and to change in spread of pain (63).

The current results of rather few sociodemographic predictors for short- to medium-term (2 years in the present study) results in CP (multivariable model 2) are, to some extent, in line with a longitudinal study on sociodemographic disparities in CP (64) and with a study in which socioeconomic status seemingly related to CP was explained by psychological factors (65). Based on the results of multivariable model 1, it is likely that the sociodemographic factors will be more predictive of long-term development or changes in CP, and this topic needs further investigation.

Traumatic injuries, RA/OA, GI disorders, pulmonary disorders, CVD and/or CNS disorders were predictors of changes in pain intensity and spread of pain in the final models in this study (Tables II and III, model 2). These comorbidities have been related to CP intensity and spread (17, 18, 33, 66) and change in intensity (45, 67) and spread of pain (68, 69). Previous studies found pulmonary diseases to be associated with pain intensity (19) and GI disorders, such as irritable bowel disease and spread of pain (70). In the current study, pulmonary and GI disorders were also predictors of pain intensity and spread of pain according to multivariable models 2, respectively. The current finding of RA/OA as predictors for the 3 pain characteristics and change in spread of pain (Table III, model 2), is in line with the findings of cross-sectional studies (71–73). Several comorbidities were predictive of pain characteristics according to both multivariable models investigated (Tables II–IV). From a clinical perspective, it appears important that the assessment of people with pain should include a broad screening of different medical conditions. From the results of the present study it can also be concluded that physical comorbidities were more important than psychological comorbidities, e.g. depressive symptoms.

Strenghts and limitations

Major strengths of this study, in terms of solid interpretations and precise estimation of predictors, are the longitudinal study design and the large sample size. The method of examining only the T0 predictors signified that any new predictor (e.g. new incidence of traumatic injury) would not be counted if it triggered different pain characteristics at T1. Therefore, the risk of single source bias was also decreased (e.g. reporting of changed life circumstances influence reporting of pain when they are done at the same time). Interestingly, strong associations were found between the baseline and the 2-year follow-up regarding pain characteristics. Nevertheless, it is important to note there was no risk of multicollinearity ($r < 0.75$) between the 3 pain characteristics.

A limitation of the current study is that the assessments of pain characteristics and comorbidities were based on self-reported instruments; nonetheless, information on self-reported comorbidities has been reported to be reliable (26). Furthermore, selective participation both at baseline and during follow-up is a concern. If participation is lower among subjects with low socioeconomic status at baseline and worse pain during follow-up, this would most likely lead to underestimations. This may also explain why common comorbidities to pain, such as depression and anxiety, in cohorts with CP (5) had insignificant influence on the pain characteristics when these baseline variables were included in the current study (i.e. multivariable model 2). The presence of certain comorbidities in the present study to a great extent depended on diagnoses made by physicians, and a recent report indicates that the prevalence of clinically assessed depression and anxiety are, in fact, relatively low compared with reported depressive and anxiety symptoms (74). The time investigated might be of importance as to whether these comorbidities, as well as the other investigator factors, are predictors. It might also be that some of the identified predictors/risk factors in the current study are due to reversed cause. For example, some pain characteristics might, to some extent, influence socioeconomic factors.

Conclusion

In planning treatment and rehabilitation, pain intensity, spread, and sensitivity should be considered, because these pain characteristics were stronger predictors of the future pain situation than were socio-demographics and co-morbidities.

ACKNOWLEDGEMENT

The Swedish Pain Foundation, Linköping University, and The Medical Research Council of Southeast Sweden contributed financially to this study. The funding bodies did not participate in the collection, analysis, and interpretation of data, the writing of the manuscript, or the decision to submit the manuscript for publication.

The authors have no conflicts of interest to declare.

REFERENCES

1. Breivik H, Collett B, Ventafridda V, Cohen R, Gallacher D. Survey of chronic pain in Europe: prevalence, impact on daily life, and treatment. Eur J Pain 2006; 10: 287–333.
2. Mundal I, Bjorngaard JH, Nilsen TI, Nicholl BI, Grawe RW, Fors EA. Long-term changes in musculoskeletal pain sites in the general population: the HUNT study. 2016; 17: 1246–1256.
3. Nakamura M, Nishiwaki Y, Ushida T, Toyama Y. Prevalence and characteristics of chronic musculoskeletal pain in Japan: a second survey of people with or without chronic pain. J Orthop Sci 2014; 19: 339–350.
4. Viniol A, Jegan N, Brugger M, Leonhardt C, Barth J, Baum E, et al. Even worse – risk factors and protective factors for transition from chronic localized low back pain to chronic widespread pain in general practice. Spine 2015; 40: E890–E899.
5. Mundal I, Gråwe RW, Bjørngaard JH, Linaker OM, Fors EA. Prevalence and long-term predictors of persistent chronic widespread pain in the general population in an 11-year prospective study: the HUNT study. BMC Musculoskelet Disord 2014; 15: 213.
6. Mundal I, Gråwe RW, Bjørngaard JH, Linaker OM, Fors EA. Psychosocial factors and risk of chronic widespread pain: an 11-year follow-up study – the HUNT study. Pain 2014; 155: 1555–1561.
7. Mork PJ, Vik KL, Moe B, Lier R, Bardal EM, Nilsen TI. Sleep problems, exercise and obesity and risk of chronic musculoskeletal pain: the Norwegian HUNT study. Eur J Public Health 2014; 24: 924–929.
8. Nordeman L, Gunnarsson R, Mannerkorpi K. Prognostic factors for work ability in women with chronic low back pain consulting primary health care: a 2-year prospective longitudinal cohort study. Clin J Pain 2014; 30: 391–398.
9. Dansie EJ, Turk DC. Assessment of patients with chronic pain. Br J Anaesth 2013; 111: 19–25.
10. Dragioti E, Larsson B, Bernfort L, Levin LA, Gerdle B. A cross-sectional study of factors associated with the number of anatomical pain sites in an actual elderly general population: results from the PainS65+ cohort. J Pain Res 2017; 10: 2009–2019.
11. Breivik H, Borchgrevink PC, Allen SM, Rosseland LA, Romundstad L, Hals EK, et al. Assessment of pain. Br J Anaesth 2008; 101: 17–24.
12. Coombes BK, Bisset L, Vicenzino B. Cold hyperalgesia associated with poorer prognosis in lateral epicondylalgia: a 1-year prognostic study of physical and psychological factors. Clin J Pain 2015; 31: 30–35.
13. Sterling M, Jull G, Vicenzino B, Kenardy J. Sensory hypersensitivity occurs soon after whiplash injury and is associated with poor recovery. Pain 2003; 104: 509–517.
14. Grimby-Ekman A, Gerdle B, Bjork J, Larsson B. Comorbidities, intensity, frequency and duration of pain, daily functioning and health care seeking in local, regional, and widespread pain – a descriptive population-based survey (SwePain). BMC Musculoskelet Disord 2015; 16: 165.
15. Al-Arfaj AS, Alballa SR, Al-Dalaan AN, Al-Saleh SS, Al-Sekeit MA, Bahabri SA, et al. Musculoskeletal pain in the community. Saudi Med J 2003; 24: 863–867.
16. Landmark T, Romundstad P, Dale O, Borchgrevink PC, Vatten L, Kaasa S. Chronic pain: one year prevalence and associated characteristics (the HUNT pain study). Scand J Pain 2013; 4: 182–187.
17. Morales-Espinoza EM, Kostov B, Salami DC, Perez ZH, Rosalen AP, Molina JO, et al. Complexity, comorbidity, and health care costs associated with chronic widespread pain in primary care. Pain 2016; 157: 818–826.
18. Parsons S, McBeth J, Macfarlane GJ, Hannaford PC, Symmons DP. Self-reported pain severity is associated with a history of coronary heart disease. Eur J Pain 2015; 19: 167–175.
19. Kurita GP, Sjogren P, Juel K, Hojsted J, Ekholm O. The burden of chronic pain: a cross-sectional survey focussing on diseases, immigration, and opioid use. Pain 2012; 153: 2332–2338.
20. Fillingim RB, Loeser JD, Baron R, Edwards RR. Assessment of chronic pain: domains, methods, and mechanisms. J Pain 2016; 17: T10–T20.
21. Von Korff M, Scher AI, Helmick C, Carter-Pokras O, Dodick DW, Goulet J, et al. United States National Pain Strategy for Population Research: concepts, definitions, and pilot data. J Pain 2016; 17: 1068–1080.
22. Larsson B, Gerdle B, Bjork J, Grimby-Ekman A. Pain Sensitivity and its relation to spreading on the body, intensity, frequency, and duration of pain: a cross-sectional population-based study (SwePain). Clin J Pain 2016; 33: 579–587.
23. von Elm E, Altman DG, Egger M, Pocock SJ, Gotzsche PC, Vandenbroucke JP. Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) statement: guidelines for reporting observational studies. BMJ 2007; 335: 806–808.
24. Dragioti E, Larsson B, Bernfort L, Levin LA, Gerdle B. Prevalence of different pain categories based on pain spreading on the bodies of older adults in Sweden: a descriptive-level and multilevel association with demographics, comorbidities, medications, and certain lifestyle factors (PainS65+). J Pain Res 2016; 9: 1131–1141.
25. Dragioti E, Bernfort L, Larsson B, Gerdle B, Levin LA. Association of insomnia severity with well-being, quality of life and health care costs: a cross-sectional study in older adults with chronic pain (PainS65+). Eur J Pain 2018; 22: 414–425.
26. Bourgeois FT, Porter SC, Valim C, Jackson T, Cook EF, Mandl KD. The value of patient self-report for disease surveillance. J Am Med Inform Assoc 2007; 14: 765–771.
27. Lundberg G, Gerdle B. The relationships between pain, disability, and health-related quality of life: An 8-year follow-up study of female home care personnel. Disabil Rehabil 2016; 38: 235–244.
28. Vasseljen O, Woodhouse A, Bjørngaard JH, Leivseth L. Natural course of acute neck and low back pain in the general population: the HUNT study. Pain 2013; 154: 1237–1244.
29. Skillgate E, Magnusson C, Lundberg M, Hallqvist J. The age- and sex-specific occurrence of bothersome neck pain in the general population – results from the Stockholm public health cohort. BMC Musculoskelet Disord 2012; 13: 185.
30. Nitter AK, Pripp AH, Forseth KØ. Are sleep problems and non-specific health complaints risk factors for chronic pain? A prospective population-based study with 17 year follow-up. Scand J Pain 2012; 3: 210–217.
31. Henschke N, Ostelo RWJG, Terwee CB, Van Der Windt DAWM. Identifying generic predictors of outcome in patients presenting to primary care with nonspinal musculoskeletal pain. Arthritis Care Res (Hoboken) 2012; 64: 1217–1224.
32. Ferreira-Valente MA, Pais-Ribeiro JL, Jensen MP. Validity of four pain intensity rating scales. Pain 2011; 152: 2399–2404.
33. MacFarlane GJ, Croft PR, Schollum J, Silman AJ. Widespread pain: is an improved classification possible? J Rheumatol 1996; 23: 1628–1632.
34. Wolfe F, Smythe HA, Yunus MB, Bennett RM, Bombardier C, Goldenberg DL, et al. The American College of Rheumatology 1990 Criteria for the Classification of Fibromyalgia. Report of the Multicenter Criteria Committee. Arthritis Rheum 1990; 33: 160–172.
35. Ruscheweyh R, Marziniak M, Stumpenhorst F, Reinholz J, Knecht S. Pain sensitivity can be assessed by self-rating:

development and validation of the Pain Sensitivity Questionnaire. Pain 2009; 146: 65–74.
36. Mokkink LB, Terwee CB, Patrick DL, Alonso J, Stratford PW, Knol DL, et al. The COSMIN study reached international consensus on taxonomy, terminology, and definitions of measurement properties for health-related patient-reported outcomes. J Clin Epidemiol 2010; 63: 737–745.
37. Sellers AB, Ruscheweyh R, Kelley BJ, Ness TJ, Vetter TR. Validation of the English language pain sensitivity questionnaire. Reg Anesth Pain Med 2013; 38: 508–514.
38. Kim HJ, Suh BG, Lee DB, Lee GW, Kim DW, Kang KT, et al. The influence of pain sensitivity on the symptom severity in patients with lumbar spinal stenosis. Pain Physician 2013; 16: 135–144.
39. McCullagh P NJ. Generalized linear models. New York: 2nd edn. Chapman and Hall; 1989.
40. RM. Ob. A caution regarding rules of thumb for variance inflation factors. Qual Quant 2007; 41: 673–690.
41. Fleiss JL LB, Paik MC. Statistical methods for rates and proportions. 3rd edn. Hoboken, NJ: Chichester: Wiley-Interscience; 2003.
42. Demmelmaier I, Asenlof P, Lindberg P, Denison E. Biopsychosocial predictors of pain, disability, health care consumption, and sick leave in first-episode and long-term back pain: a longitudinal study in the general population. Int J Behav Med 2010; 17: 79–89.
43. Dunn KM, Jordan KP, Croft PR. Contributions of prognostic factors for poor outcome in primary care low back pain patients. Eur J Pain 2011; 15: 313–319.
44. Thomtén J, Soares JJF, Sundin O. The role of psychosocial factors in the course of pain-a 1-year follow-up study among women living in Sweden. Arch Womens Ment Health 2011; 14: 493–503.
45. Atherton K, Wiles NJ, Lecky FE, Hawes SJ, Silman AJ, Macfarlane GJ, et al. Predictors of persistent neck pain after whiplash injury. Emerg Med J 2006; 23: 195–201.
46. Solidaki E, Chatzi L, Bitsios P, Coggon D, Palmer KT, Kogevinas M. Risk factors for new onset and persistence of multi-site musculoskeletal pain in a longitudinal study of workers in Crete. Occup Environ Med 2013; 70: 29–34.
47. Neupane S, Miranda H, Virtanen P, Siukola A, Nygård CH. Do physical or psychosocial factors at work predict multi-site musculoskeletal pain? A 4-year follow-up study in an industrial population. Int Arch Occupat Envir Health 2013; 86: 581–589.
48. Nordeman L, Gunnarsson R, Mannerkorpi K. Prevalence and characteristics of widespread pain in female primary health care patients with chronic low back pain. Clin J Pain 2012; 28: 65–72.
49. Kindler LL, Jones KD, Perrin N, Bennett RM. Risk factors predicting the development of widespread pain from chronic back or neck pain. J Pain 2010; 11: 1320–1328.
50. Artus M, Campbell P, Mallen CD, Dunn KM, van der Windt DA. Generic prognostic factors for musculoskeletal pain in primary care: a systematic review. BMJ Open 2017; 7: e012901.
51. Gerdle B, Ghafouri B, Ghafouri N, Backryd E, Gordh T. Signs of ongoing inflammation in female patients with chronic widespread pain: a multivariate, explorative, cross-sectional study of blood samples. Medicine (Baltimore) 2017; 96: e6130.
52. Olausson P, Ghafouri B, Ghafouri N, Gerdle B. Specific proteins of the trapezius muscle correlate with pain intensity and sensitivity – an explorative multivariate proteomic study of the trapezius muscle in women with chronic widespread pain. J Pain Res 2016; 9: 345–356.
53. Aggarwal VR, Macfarlane TV, Macfarlane GJ. Why is pain more common amongst people living in areas of low socio-economic status? A population-based cross-sectional study. Br Dent J 2003; 194: 383–387; discussion 380.
54. Fernández-De-Las-Peñas C, Alonso-Blanco C, Hernández-Barrera V, Palacios-Ceña D, Jiménez-García R, Carrasco-Garrido P. Has the prevalence of neck pain and low back pain changed over the last 5 years? A population-based national study in Spain. Spine J 2013; 13: 1069–1076.
55. Viniol A, Jegan N, Leonhardt C, Brugger M, Strauch K, Barth J, et al. Differences between patients with chronic widespread pain and local chronic low back pain in primary care – a comparative cross-sectional analysis. BMC Musculoskel Dis 2013; 14: 351.
56. Neville A, Peleg R, Singer Y, Sherf M, Shvartzman P. Chronic pain: a population-based study. Isr Med Assoc J 2008; 10: 676–680.
57. Azevedo LF, Costa-Pereira A, Mendonça L, Dias CC, Castro-Lopes JM. Epidemiology of chronic pain: a population-based nationwide study on its prevalence, characteristics and associated disability in Portugal. J Pain 2012; 13: 773–783.
58. Andorsen OF, Ahmed LA, Emaus N, Klouman E. High prevalence of chronic musculoskeletal complaints among women in a Norwegian general population: the Tromsø study. BMC Research Notes 2014; 8: 506.
59. Kim C, Kim H, Kim J. Prevalence of chronic widespread pain and fibromyalgia syndrome: a Korean hospital-based study. Rheumatol Int 2012; 32: 3435–3442.
60. Arvidsson I, Gremark Simonsen J, Dahlqvist C, Axmon A, Karlson B, Bjork J, et al. Cross-sectional associations between occupational factors and musculoskeletal pain in women teachers, nurses and sonographers. BMC Musculoskelet Disord 2016; 17: 35.
61. Bergman S. Psychosocial aspects of chronic widespread pain and fibromyalgia. Disabil Rehabil 2005; 27: 675–683.
62. Cimmino MA, Ferrone C, Cutolo M. Epidemiology of chronic musculoskeletal pain. Best Pract Res Clin Rheumatol 2011; 25: 173–183.
63. Kamaleri Y, Natvig B, Ihlebaek CM, Benth JS, Bruusgaard D. Change in the number of musculoskeletal pain sites: a 14-year prospective study. Pain 2009; 141: 25–30.
64. Grol-Prokopczyk H. Sociodemographic disparities in chronic pain, based on 12-year longitudinal data. Pain 2017; 158: 313–322.
65. Davies KA, Silman AJ, Macfarlane GJ, Nicholl BI, Dickens C, Morriss R, et al. The association between neighbourhood socio-economic status and the onset of chronic widespread pain: results from the EPIFUND study. Eur J Pain 2009; 13: 635–640.
66. Burns JW, Quartana PJ, Bruehl S, Janssen I, Dugan SA, Appelhans B, et al. Chronic pain, body mass index and cardiovascular disease risk factors: tests of moderation, unique and shared relationships in the Study of Women's Health Across the Nation (SWAN). J Behav Med 2015; 38: 372–383.
67. Croft PR, Lewis M, Papageorgiou AC, Thomas E, Jayson MI, Macfarlane GJ, et al. Risk factors for neck pain: a longitudinal study in the general population. Pain 2001; 93: 317–325.
68. McBeth J, Symmons DP, Silman AJ, Allison T, Webb R, Brammah T, et al. Musculoskeletal pain is associated with a long-term increased risk of cancer and cardiovascular-related mortality. Rheumatol (Oxford) 2009; 48: 74–77.
69. Jones GT, Nicholl BI, McBeth J, Davies KA, Morriss RK, Dickens C, et al. Role of road traffic accidents and other traumatic events in the onset of chronic widespread pain: results from a population-based prospective study. Arthritis Care Res (Hoboken) 2011; 63: 696–701.
70. Kato K, Sullivan PF, Evengård B, Pedersen NL. Chronic widespread pain and its comorbidities: a population-based study. Arch Intern Med 2006; 166: 1649–1654.
71. Cho NH, Kim I, Lim SH, Kim HA. Prevalence of widespread pain and its influence on quality of life: population study in Korea. J Korean Med Sci 2012; 27: 16–21.
72. Fernández-De-Las-Peñas C, Hernández-Barrera V, Alonso-Blanco C, Palacios-Ceña D, Carrasco-Garrido P, Jiménez-Sánchez S, et al. Prevalence of neck and low back pain in community-dwelling adults in Spain: a population-based national study. Spine 2011; 36: E213–E219.
73. Lee KH, Kim CH, Shin HC, Sung EJ. Clinical characteristics of patients with medically unexplained chronic widespread pain: a primary care center study. Korean J Fam Med 2011; 32: 277–284.
74. Sondergard S, Vaegter HB, Erlangsen A, Stenager E. Ten-year prevalence of mental disorders in patients presenting with chronic pain in secondary care: a register linkage cohort study. Eur J Pain 2018; 22: 346–354.