ORIGINAL RESEARCH

Mediators of Pain and Physical Function in Female and Male Patients with Chronic Pain

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Purpose: Chronic pain is often multifactorial and accompanied by psychological distress, catastrophizing thoughts, reduced physical function, and socio-economic worries. In this explorative study, we investigated potential mediators in the relationships of psychological and demographic variables with chronic pain and physical function in women and men.

Patients and Methods: The study included 301 patients admitted to a multidisciplinary pain clinic. Prior to their first consultation, patients completed a questionnaire including items on demographics (age, education, occupational and financial situation), catastrophizing thoughts, psychological distress, pain intensity, and physical function. Hierarchical multiple regression analyses examined demographic and psychological factors associated with pain intensity and physical function. Mediation and reversed mediation models were tested and developed based on calculated relations in the regression analyses between demographic, psychological, pain intensity and physical function variables.

Results: Fifty-eight percent were females and mean age 43.8 and 46.0 years for women and men, respectively. In the regression analyses, psychological factors accounted better for pain intensity than demographic variables, while physical function was best accounted for by demographic variables. Among women, catastrophizing thoughts mediated significantly the relationships between education and pain intensity, and between education and physical function. Psychological distress mediated significantly the relationships between financial situation and pain intensity, and between financial situation and physical function in women. In men, the only significant mediation model was psychological distress mediating the relationship between financial situation and pain intensity. Some of the reversed models revealed indirect effects, indicating bidirectionality.

Conclusion: The results indicate that there might be gender-specific mediators in how demographic variables are associated with pain intensity and physical function. This suggests an awareness among clinicians of potential gender-specific factors mediating pain problems, and the need for a gender-specific, multidisciplinary approach in the treatment of chronic pain.

Keywords: depression, physical disability, comorbidity, catastrophizing, mediation, multidisciplinary treatment

Introduction

Clinical and experimental studies have documented that women are more prone to pain compared with men.[1–5] The sex hormones play a role and the effect seems to be regulated by immunological mediators.[6,7] However, chronic pain is a complex condition and several psychosocial characteristics have been identified as risk factors,[8–11] and these may also explain the gender-related differences.[12–14]

Comorbidity of pain and depressive symptoms is associated with poorer prognosis and more disability than either condition alone,[15,16] and this is found to be more

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pronounced among women compared with men.[17] In a review, including 105 epidemiological studies of recurrent pain, women experienced more recurrent pain, longer pain duration, more severe pain intensity, and they were more vulnerable to psychosocial factors than men.[18] In an epidemiological Canadian survey based on data from a national database with more than 131 000 adults, depressive symptoms and chronic pain were twice as prevalent in women as in men, and comorbidity of depression and pain was significantly associated with psychological distress and disability among women.[17] In another large population-based study from 13 European countries, women with chronic pain were also more prone to report depressive symptoms than men with chronic pain. Treatment of depressive symptoms interestingly seemed to protect from persistent pain among women but not among men.[19] When Keefe et al in pre-treatment data from two randomized, clinical treatment studies (N: 168) found relatively higher pain levels and worse physical function among women than men suffering from osteoarthritis, catastrophizing thoughts mediated the relation between gender and pain outcomes.[20]

Clinical outcome of patients being treated for chronic pain varies. A large Finnish follow-up study of patients (N=1043) subjected to multidisciplinary treatment addresses the need for more research on factors which are associated with improved health-related quality of life in order to understand why some patients don´t benefit from multidisciplinary treatment.[21] When treating patient with severe chronic pain Hysing et al argue for increased awareness of the huge burden of symptoms additional to pain, and particularly psychiatric comorbidity and low physical functioning.[22] Since chronic pain and health problems are closely associated with socioeconomic status,[23–26] factors like education and economy and potential associations with psychological factors need to be included in the study of chronic pain.

Considering the biological gender differences and the complex and multifactorial nature of chronic pain, we hypothesized that psychological distress and negative cognitions mediate the relations between demographic factors and pain intensity and physical function. In this explorative study, we, therefore, performed separate analyses for men and women and also tested for potential bidirectional[27] mediation by psychological distress and catastrophizing thoughts on demographic factors and pain intensity as well as physical function. If different mediators could be identified in women and men, this would imply the need for further research on this topic which might have important clinical implications for future treatment of chronic pain.

Materials and Methods
Participants
Patients admitted to the Multidisciplinary Pain Clinic at the University Hospital of North Norway (UNN) in the period of 2010–2012, were included in the study. All referrals were evaluated by a multidisciplinary team before being accepted for admittance. The same criteria to be accepted were used for all referrals. The clinic admitted patients with a non-malignant complex chronic pain condition. The project included all patients admitted to the clinic.

Design
In this cross-sectional designed study, data were collected by a set of self-reported questionnaire routinely completed by all patients admitted to the clinic as part of the clinical assessment. The questionnaire was attached to the invitation letter for hospital admittance sent to the patients by mail, in a paper-and-pencil format, and completed by the patients prior to their first consultation.[28]

Methods
Ethics
The study was part of a quality assurance project approved by the Data Protection Official at UNN (Project no 0084/ Ref2008/4213-1), and exempted from patient consent according to the Norwegian Health Personnel Act.

Measures
The set of questionnaires, including validated and internationally acknowledged instruments, was compiled and recommended by the Norwegian Association of Pain for use in Norwegian Pain Clinics. The variables applied in this study include:

Demographics: Gender, age, total years of education (dichotomized into ≤12 or >12 years), working/in education status ("work status") (dichotomized to yes= full or part-time work or study, no= no work or study). Perceived financial situation: How do you perceive your financial situation? Three answer options (poor, medium and good) which was dichotomized into poor or medium/good.

Pain assessment: Most severe, least severe, and average pain intensities during the last week were assessed by 11-point numeric rating scales (NRS) ranging from 0 to 10 where 0 = no pain and 10 = worst possible pain. The pain scales originate from the Brief Pain Inventory (BPI) and have shown satisfactory properties.[29,30] In this study, pain intensity was presented as an average of the scores from the three pain assessment scales.

Catastrophizing thoughts: Two items from the catastrophizing subscale of the Coping Strategies Questionnaire (CSQ) were included to assess tendencies for catastrophizing thoughts: 1. "When I feel pain it is terrible, and I feel it is never going to get any better". 2. "When I feel pain, I feel I can't stand it anymore." Response format was a 7-point scale (0–6 where 0 = never and 6 = always). These items have proved useful for clinical purposes in the initial screening and treatment monitoring.[31] The two-item version of CSQ provides adequately valid estimates of catastrophizing, due to the strong associations with the original scales and their sensitivity to changes with treatment.[32]

Physical function: The 10 questions originate from the health domain on physical function in the Norwegian version of the RAND 36-Item Short Form Health Survey.[33] Physical function captures both the presence and extent of physical limitations, applying a three-level response format, ranging from 1 to 3 (1= yes, limited a lot, 2= yes, limited a little, 3= no, not limited at all). The scores are converted into 0–100 scales (0 = worst possible physical function, 100 = best possible physical function).

Psychological distress: The Hopkins Symptom Checklist-25 (HSCL-25) is a widely used, self-administrated instrument. It is based on the main symptom dimensions of depression and anxiety and is a valid and reliable measure of psychological distress.[34] The questionnaire contains 25 items with 4-point scales response format ranging from 1 = not at all to 4 = extremely. The average item score is calculated by dividing the total score by the number of items answered.[35,36] A cut-off point of 1.75 for women and 1.67 for men have been suggested as a valid predictor of psychological distress.[34,36,37] Items missing were imputed according to the Expectation Maximization (EM) algorithm provided by the SPSS.[38] Only patients completing a minimum of 20 of the 25 items, were included.

Statistical Methods

All data were analysed using SPSS for Windows version 24. For bivariate analyses, Pearson's product-moment correlations were examined for continuous independent and dependent variables (age, psychological distress, catastrophizing, pain and physical function). Phi correlations were applied to examine dichotomous variables (work status, perceived financial situation and education) while point-biserial correlations examined the strength of the association between dichotomous (work status, financial situation and education) and continuous variables (age, psychological distress, catastrophizing, pain and physical function). The bivariate analyses were separated by gender.

First, hierarchical regression analyses examined the associations among variables of relevance based on previous clinical research. Then, mediation models, based on the regression results, were developed and tested.

The hierarchical multiple regressions analyzed the main effects of the independent variables age, education, work status, perceived financial position, psychological distress and catastrophizing thoughts on the two dependent variables pain intensity and physical function for men and women, respectively. To identify and differentiate the effects of demographics and psychological factors, they were entered into the regression in respective blocks. Demographic factors (age, education, work status and perceived financial situation) were entered into block 1, followed by psychological factors (psychological distress and catastrophizing thoughts) into block 2.

To explore potential mediating effects of psychological distress and catastrophizing thoughts, mediation models were developed based on the observed significant relations in the regression analyses. Models for women and men were created and tested separately. Alternative, reversed models were tested due to potential reversed directionality of the mediations. In these reversed models, the dependent variable was defined as the mediating variable and the mediating variable as dependent variable. The mediation analyses separated the direct and indirect effects, which could be essential for establishing new relevant hypotheses on causality. Due to alike analysis schemes, we chose a mediation approach similar to what was described by Newman et al,[27] applying Hayes' SPSS macro, PROCESS with 5000 bootstrap resampling. Bootstrapping is a nonparametric resampling procedure that does not assume multivariate normality.[39,40] We estimated 95% bias-corrected and accelerated (BCa) bootstrapped confidence intervals and point estimates. When the corresponding bootstrapped confidence intervals did not contain zero, the indirect effect was considered statistically significant.[40] The analyses were performed in accordance with recommendations from statisticians at the institution.

Results
Demographics

The sample included the complete patient population admitted to the pain clinic during a two-year time-period; a total of 301 patients. Two thirds were referred from general practitioners and one third from physicians at hospitals. The same criteria to be accepted were used for all referrals. The patients had experienced pain for a notable period of time (91% > 1 year, 37% >10

years). The criteria[41] for widespread pain was fulfilled by 45% (135) patients, of them 65% (88) were women. Mean age was 45 years (SD 13.4) and 58% (176) were females. Higher education (>12 years) was reported by 24% (72), 72% (209) were out of work, and 66% (194) perceived their financial situation as average or good. We found moderately high levels of pain intensity (mean=6.0, SD=1.76), and relatively high levels of psychological distress (2.0, SD=0.59) and catastrophizing thoughts (mean=3.8, SD=1.4), while physical function was relatively low with a mean of less than 50% of full score (mean=49, SD=25). Sample characteristics are presented separately for each gender in Table 1.

In bivariate correlations among women, we found strong (r>0.50) associations between psychological distress and pain intensity, and catastrophizing thoughts and pain intensity, medium (r=0.30 to 0.49) associations between age and physical function, work status and physical function, psychological distress and pain intensity, and between pain intensity and physical function. In men, we found medium (r=0.30 to 0.49) associations between psychological distress and pain intensity, catastrophizing thoughts and pain intensity, pain intensity and physical function, financial situation and psychological distress, and between psychological distress and catastrophizing thoughts. Some additional associations were statistically significant, but weak. The gender-specific bivariate correlations are presented in Tables 2 and 3.

Hierarchical Multiple Regressions
Regression Analyses of Pain Intensity and Physical Function Among Women
The first regression model examined the dependent variable pain intensity among women. When age, work status, perceived financial situation, and education were entered in block 1, only age and education remained statistically significant predictors. Adding psychological distress and catastrophizing thoughts in block 2 resulted in a model with education and catastrophizing thoughts as significant predictors. In this model ($F_{(6,157)}= 14.32$, $p<0.001$) demographic variables explained 11.6% and psychological variables 23.8% of the variance of pain intensity among women (Table 4).

In the second regression model, the dependent variable physical function among women was examined. Age, work status, perceived financial situation, and education were entered in block 1. Here, age, work status, and perceived financial situation remained significant predictors. Adding psychological distress and catastrophizing thoughts in block 2 resulted in a model with age, work status, and catastrophizing thoughts as significant predictors. In this model ($F_{(6,160)} =8.26$, $p<0.001$) demographic variables explained 17.8% and psychological variables 5.9% of the variance of physical function among women (Table 4).

Regression Analyses of Pain Intensity and Physical Function Among Men
The first regression model examined the dependent variable pain intensity among men. When age, work status, perceived financial situation, and education were entered in block 1, age remained a significant predictor. Adding psychological distress and catastrophizing thoughts in block 2 resulted in a model with education, psychological distress, and catastrophizing thoughts as significant predictors. In the model ($F_{(6,107)}= 10.23$, $p<0.001$) demographic variables explained 10.6% and psychological variables 25.8% of the variance of pain intensity among men (Table 5).

Table 1 Sample Characteristics

	Women N=176 Mean (SD)	Women N	Men N=125 Mean (SD)	Men N
Age (years)	43.8 (14.3)	176	46.0 (11.9)	125
Psychological distress	2.02(0.59)	172	1.96(0.59)	119
Catastrophizing	3.9(1.4)	172	3.66(1.4)	120
Pain	6.1(1.9)	169	5.9(1.6)	122
Physical function	48.0(25.4)	174	51.1(24.0)	123
	(%)		(%)	
Work status (not working)	69.8	172	74.8	119
Perceived financial situation (average or good)	70.0	170	61.0	123
Education (< 12 years)	76.0	175	75.8	124

Abbreviations: Psychological distress: HopkinsSymptom Check List-25 (Range:1-4), Catastrophizing thoughts: Coping Strategies Questionnaire (Range: 0-6), Pain intensity (Numeric Rating Scale,0-10), Physical function: RAND 36 (Range: 0-100).

Table 2 Bivariate Correlations Among Study Variables (Women)

Variables	Age	Work Status	Financial Situation	Education	Psychological Distress	Catastrophizing	Pain	Physical Function
Age	–	–	–	–	–	–	–	–
Work status	0.299**	–	–	–	–	–	–	–
Financial situation	0.255**	0.134	–	–	–	–	–	–
Education	−0.018	0.167*	0.077	–	–	–	–	–
Psychological distress	−0.005	−0.085	−0.196*	−0.052	–	–	–	–
Catastrophizing	0.105	−0.057	−0.134	−0.174*	0.501**	–	–	–
Pain	0.207**	−0.174*	−0.073	−0.244**	0.340**	0.542**	–	–
Physical function	0.321**	0.308**	0.116	0.034	−0.220**	−0.287**	−0.463**	–

Notes: *Statistical significance with a p-value <0.05. **Statistical significance with a p-value <0.01.
Abbreviations: Psychological distress: Hopkins Symptom Check List–25, Catastrophizing thoughts: Coping Strategies Questionnaire, Pain: Pain intensity (Numeric Rating Scale), Physical function: Subscale of RAND 36.

Table 3 Bivariate Correlations Among Study Variables (Men)

Variables	Age	Work Status	Financial Situation	Education	Psychological Distress	Catastrophizing	Pain	Physical Function
Age	–	–	–	–	–	–	–	–
Work status	−0.148	–	–	–	–	–	–	–
Financial situation	0.228*	0.244**	–	–	–	–	–	–
Education	0.124*	0.009	0.052	–	–	–	–	–
Psychological distress	−0.016	−0.148	−0.354**	0.084	–	–	–	–
Catastrophizing	0.042	0.080	−0.132	0.046	0.414**	–	–	–
Pain	0.162	−0.214*	−0.180*	−0.099	0.481**	0.418**	–	–
Physical function	−0.177	0.189*	0.252**	0.068	−0.298**	−0.297**	−0.309**	–

Notes: *Statistical significance with a p-value <0.05. **Statistical significance with a p-value <0.01.
Abbreviations: Psychological distress: Hopkins Symptom Check List–25, Catastrophizing thoughts: Coping Strategies Questionnaire, Pain: Pain intensity (Numeric Rating Scale), Physical function: Subscale of RAND 36.

The second model examined the dependent variable physical function among men. When age, work status, perceived financial situation, and education were entered in block 1, age and perceived financial situation remained significant predictors. Adding psychological distress and catastrophizing thoughts in block 2 resulted in a model with age and catastrophizing thoughts as significant predictors. In the model ($F_{(6,107)}$=4.99, p<0.001) demographic variables explained 13.5% and psychological variables 8.4% of the variance of physical function among men (Table 5).

Regression Analyses of Catastrophizing Thoughts and Psychological Distress in Women and Men

The first regression model examined associations between the dependent variable catastrophizing thoughts and demographic factors in woman and men, respectively. Age, work status, perceived financial situation and education were included as independent variables. Perceived financial situation and education remained significant predictors among women ($F_{(4,162)}$=2.82, p=0.027), and the demographic variables explained 6.5% of the variance of catastrophizing thoughts among women. None of the demographic variables were significantly associated with catastrophizing thoughts among men (Tables 6 and 7).

Thesecond regression model examined associations between the dependent variable psychological distress and demographic factors for women and men, respectively. When age, work status, perceived financial situation, and education were entered, only perceived financial situation remained a significant predictor, both in the model for women and in the one for men. In the model, demographic variables explained 14.1% of the variance of psychological distress among men ($F_{(4,110)}$=4,53, p=0.002), for women the model was non-significant ($F_{(4,162)}$=1,84, p=0.123) (Tables 6 and 7).

Mediation (Figure 1)

Based on relations established in the regressions, we examined a series of 11 mediation models among women and 6 models among men (Tables 6 and 7). The criterion for

Table 4 Summary of Multiple Regression Analyses of Pain and Physical Function in Women

	Predictor	ΔR^2	B	SE	Std B	p	95% CI for B	
Pain							Lower	Upper
Step 1		0.116**						
	Age		0.028	0.011	0.211	0.011	0.006	0.049
	Work status		-0.247	0.330	-0.061	0.456	-0.898	0.405
	Financial situation		-0.412	0.323	-0.101	0.204	-1.049	0.226
	Education		-0.971	0.331	-0.222	0.004	-1.624	-0.317
Step 2		0.238**						
	Age		0.018	0.009	0.139	0.055	0.000	0.037
	Work status		-0.299	0.285	-0.074	0.296	-0.861	0.264
	Financial situation		-0.029	0.283	-0.007	0.919	-0.589	0.531
	Education		-0.637	0.289	-0.146	0.029	-1.208	-0.066
	Psychological distress		0.326	0.239	0.102	0.175	-0.147	0.798
	Catastrophizing		0.598	0.102	0.445	0.000	0.396	0.800
Physical function								
Step 1		0.178***						
	Age		-0.545	0.140	-0.306	0.000	-0.821	-0.269
	Work status		10.833	4.283	0.196	0.012	2.377	19.290
	Financial function		9.335	4.189	0.169	0.027	1.062	17.608
	Education		-0.988	4.295	-0.017	0.818	-9.470	7.493
Step 2		0.059**						
	Age		-0.486	0.137	-0.273	0.001	-0.757	-0.214
	Work status		11.050	4.165	0.200	0.009	2.824	19.275
	Financial situation		6,.04	4.146	0.119	0.113	-1.584	14.792
	Education		-3.066	4.230	-0.052	0.470	-11.421	5.288
	Psychological distress		-3.660	3.500	-0.085	0.297	-10.573	3.253
	Catastrophizing		-3.602	1.497	-0.197	0.017	-6.559	-0.646

Notes: **Statistical significance with a p-value <0.01, ***Statistical significance with a p-value <0.001
Abbreviations: Psychological distress: Hopkins Symptom Check List–25, Catastrophizing thoughts: Coping Strategies Questionnaire, Pain: Pain intensity (Numeric Rating Scale), Physical function: Subscale of RAND 36.

selecting these variables was a statistically significant association between the independent and dependent variable. Furthermore, following the arguments provided by Preacher and Hayes,[40] a significant association between independent (X) and dependent variables (Y) is not necessary for considering a mediation analysis. Thus, among the female models, we also included perceived financial situation due to the statistically significant relationship with the mediator variables (M) catastrophizing and psychological distress. Among the male models, we included perceived financial situation due to the statistically significant relationship with the mediator variable psychological distress.

Due to potential bidirectionality, alternative reversed models were tested. In these models, pain intensity and physical function were mediators (M) and the psychological variables (psychological distress and catastrophizing thoughts) dependent variables (Y).

Mediation Results in Women

The models 1–6 (Table 8) among women examined catastrophizing thoughts (M) as a potential mediator. Two of the six tested models with catastrophizing thoughts (M) as mediator were statistically significant. The indirect effects showed that catastrophizing thoughts (M) fully mediated the relationship between education (X) and physical function (Y) (model number 6), and partially between education (X) and pain intensity (Y) (model number 2). The models 7–11 examined psychological distress (M) as a potential mediator (Table 6). Two of the five tested models with psychological distress (M) as mediator

Table 5 Summary of Multiple Regression Analyses of Pain and Physical Function in Men

	Predictor	ΔR²	B	SE	Std B	p	95% CI for B	
Pain							Lower	Upper
Step 1		0.106*						
	Age		0.027	0.013	0.198	0.041	0.001	0.052
	Work status		-0.507	0.351	-0.138	0.152	-0.202	0.189
	Financial situation		-0.605	0.317	-0.185	0.059	-1.234	0.024
	Education		-0.420	0.340	-0.113	0.219	-1.093	0.253
Step 2		0.258***						
	Age		0.021	0.011	0.153	0.064	-0.001	0.043
	Work status		-0.582	0.304	-0.159	0.058	-1.184	0.020
	Financial situation		-0.015	0.287	-0.005	0.957	-0.584	0.553
	Education		-0.593	0.291	-0.159	0.044	-1.169	-0.017
	Psychological distress		0.970	0.248	0.355	0.000	0.477	1.462
	Catastrophizing		0.321	0.097	0.284	0.001	0.128	0.514
Physical function								
Step 1		0.135*						
	Age		-0.483	0.191	-0.239	0.013	-0.862	-0.104
	Work status		4.634	5.189	0.084	0.374	-5.651	14.919
	Financial function		13.827	4.692	0.282	0.004	4.528	23.127
	Education		4.609	5.023	0.082	0.361	-5.346	14.565
Step 2		0.084*						
	Age		-0.425	0.184	-0.210	0.023	-0.790	-0.060
	Work status		5.942	5.060	0.108	0.243	-4.088	15.973
	Financial situation		9.390	4.783	0.191	0.052	-0.091	18.872
	Education		5.863	4.844	0.105	0.229	-3.739	15.465
	Psychological distress		-5.546	4.139	-0.135	0.183	-13.752	2.660
	Catastrophizing		-3.755	1.624	-0.221	0.023	-6.975	-0.536

Notes: *Statistical significance with a p-value <0.05, ***Statistical significance with a p-value <0.001.
Abbreviations: Psychological distress: Hopkins symptom check list–25, Catastrophizing thoughts: Coping Strategies Questionnaire, Pain: Pain intensity (Numeric rating Scale), Physical function: Subscale of RAND 36.

Table 6 Summary of Multiple Regression Analyses of Catastrophizing and Psychological Distress Variables in Women

	Predictor	ΔR²	B	SE	Std B	p	95% CI for B	
Catastrophizing							Lower	Upper
		0.065*						
	Age		0.015	0.008	0.156	0.064	-0.001	0.031
	Work status		0.118	0.250	0.039	0.638	-0.376	0.612
	Financial situation		-0.504	0.245	-0.166	0.041	-0.987	-0.020
	Education		-0.536	0.251	-0.165	0.034	-1.031	-0.041
Psychological distress								
		0.044						
	Age		0.001	0.003	0.031	0.711	-0.006	0.008
	Work status		-0.057	0.107	-0.045	0.595	-0.268	0.,154
	Financial function		-0.251	0.105	-0.196	0.018	-0.457	-0.044
	Education		-0.040	0.107	-0.029	0.708	-0.252	0.172

Notes: *Statistical significance with a p-value <0.05.
Abbreviations: Psychological distress: Hopkins symptom check list–25, Catastrophizing thoughts: Coping Strategies Questionnaire.

Table 7 Summary of Multiple Regression Analyses of Catastrophizing and Psychological Distress Variables in Men

	Predictor	ΔR^2	B	SE	Std B	p	95% CI for B	
Catastrophizing							Lower	Upper
		0.043						
	Age		0.12	0.012	0.102	0.308	-0.011	0.035
	Work status		0.458	0.321	0.141	0.156	-0.178	1,093
	Financial situation		-0.554	0.290	-0.192	0.058	-1,129	0.020
	Education		0.138	0.310	0.042	0.658	-0.477	0.753
Psychological distress								
		0.141**						
	Age		0.002	0.005	0.045	0.633	-0.007	0.011
	Work status		-0.074	0.125	-0.055	0.555	-0.322	0.174
	Financial function		-0.425	0.113	-0.355	0.000	-0.649	-0.200
	Education		0.133	0.121	0.097	0.276	-0.108	0.373

Notes: **Statistical significance with a p-value < 0.01.
Abbreviations: Psychological distress: Hopkins symptom check list-25, Catastrophizing thoughts: Coping Strategies Questionnaire.

were statistically significant. The indirect effects showed that psychological distress (M) fully mediated the relationship between perceived financial situation (X) and physical function (Y) (model number 7), and also fully between perceived financial situation (X) and pain intensity (Y) (model number 8). The other models were not statistically significant (Table 8).

When reversing the significant models (numbers 2, 6, 7 and 8), pain intensity (M) and physical function (M) were defined as mediators and catastrophizing thoughts (Y) and psychological distress (Y) as dependent variables (Table 9). One of the 2 tested models with pain intensity (M) as mediator was statistically significant (model number 2). The indirect effects confirmed that pain intensity (M) fully mediated the relation between education (X) and catastrophizing thoughts (Y). None of the two tested models with physical function (M) as mediator were statistically significant (Table 9).
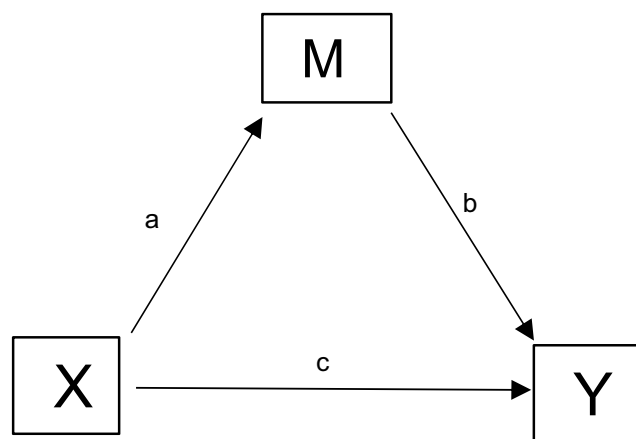

Figure I Indirect effect of X on Y through M=ab. Direct effect of X on Y=c.

Mediation Results in Men

Model number 1 for men examined catastrophizing thoughts (M) as a potential mediator. However, this model was not statistically significant. The models 2–6 examined psychological distress (M) as a potential mediator (Table 10), and one of these five tested models was statistically significant. The indirect effect showed that psychological distress (M) fully mediated the relationship between perceived financial situation (X) and pain intensity (Y) (model number 2). None of the other models were statistically significant (Table 10).

When reversing the significant model (number 2), pain intensity (M) was defined as mediator and psychological distress (Y) as dependent variables (Table 11), and the model was statistically significant (Table 11). The indirect effect confirmed that pain intensity (M) partially mediated the relation between perceived financial situation (X) and psychological distress (Y).

Discussion

The comorbidity of psychological distress and chronic pain, and how these health problems are associated with socioeconomic status are well documented.[23–26] This study confirms these associations and brings further the knowledge of these issues by identifying psychological mediators of these associations. Our results show that catastrophizing thoughts may contribute to increased pain perception in women, not only as a direct relationship as shown by others,[42–44] but also as a mediator explaining how other factors are related to pain and physical function. In this way, the results confirm the

Table 8 Summary of Mediation Models with Catastrophizing and Psychological Distress as Mediators in Women, Based on 5000 Bootstrap Samples

	Independent Variable	Mediating Variable	Dependent Variable	Direct Effects	Indirect Effects	Bootstrapping BCa 95% CI	
						Lower	Upper
1.	Financial situation	Catastrophizing	Pain	0.0342	−0.3310	−0.6968	0.0137
2.	**Education**	**Catastrophizing**	**Pain**	**−0.6739***	**−0.3856***	**−0.7332**	**−0.0728**
3.	Age	Catastrophizing	Physical function	−0.5200*	−0.0482	−0.1344	0.0150
4.	Work status	Catastrophizing	Physical function	15.4819*	0.8581	−0.4333	3.3223
5.	Financial situation	Catastrophizing	Physical function	3.7811	2.1329	−0.3581	5.0148
6.	**Education**	**Catastrophizing**	**Physical function**	**−0.4501**	**2.9523***	**0.4952**	**6.5380**
7.	**Financial situation**	**Psychological distress**	**Physical function**	**3.5381**	**2.2183***	**0.1604**	**5.2661**
8.	**Financial situation**	**Psychological distress**	**Pain**	**0.0411**	**−0.2926***	**−0.6019**	**−0.0579**
9.	Education	Psychological distress	Pain	−1.1086*	−0.0554	−0.2947	0.1464
10.	Work status	Psychological distress	Physical function	14.9610*	0.9097	−0.7734	2.9234
11.	Age	Psychological distress	Physical function	−0.5608*	0.0018	−0.0579	0.0697

Notes: BCa indicates bias-corrected and accelerated. *Statistically significant point estimate (p-value < 0.05).
Abbreviations: Catastrophizing thoughts: Coping Strategies Questionnaire, Psychological distress: Hopkins Symptom Check List-25, Pain: Pain intensity (Numeric Rating Scale), Physical function: Subscale of RAND 36. Significant results in bold font.

Table 9 Summary of Reversed Mediation Models (The Significant Models from Table 8) with Pain and Physical Function as Mediators in Women, Based on 5000 Bootstrap Samples

	Independent Variable	Mediating Variable	Dependent Variable	Direct Effects	Indirect Effects	Bootstrapping BCa 95% CI	
						Lower	Upper
2.	**Education**	**Pain**	**Catastrophizing**	**−0.1375**	**−0.4141***	**−0.7071**	**−0.1576**
6.	Education	Physical function	Catastrophizing	−0.5238*	−0.0384	−0.1839	0.1010
7.	Financial situation	Physical function	Psychological distress	−0.2225*	−0.0270	−0.0796	0.0128
8.	Financial situation	Pain	Psychological distress	−0.2448*	−0.0255	−0.1025	0.0440

Notes: BCa indicates bias-corrected and accelerated. *Statistically significant point estimate (p-value < 0.05).
Abbreviations: Catastrophizing thoughts: Coping Strategies Questionnaire, Psychological distress: Hopkins Symptom Check List-25, Pain: Pain intensity (Numeric Rating Scale), Physical function: Subscale of RAND 36. Significant results in bold font.

Table 10 Summary of Mediation Models with Catastrophizing and Psychological Distress as Mediators in Men, Based on 5000 Bootstrap Samples

	Independent Variable	Mediating Variable	Dependent Variable	Direct Effects	Indirect Effects	Bootstrapping BCa 95% CI	
						Lower	Upper
1.	Age	Catastrophizing	Physical function	−0.3400	−0.0247	−0.1608	0.0686
2.	**Financial situation**	**Psychological distress**	**Pain**	**−0.1352**	**−0.5495***	**−0.9306**	**−0.2420**
3.	Education	Psychological distress	Pain	−0.4694	0.1412	−0.1530	0.5002
4.	Age	Psychological distress	Physical function	−0.2730	0.0095	−0.1070	0.1048
5.	Education	Psychological distress	Pain	−0.4694	0.1412	−0.1690	0.5008
6.	Age	Psychological distress	Physical function	−0.2730	0.0095	−0.1024	0.1024

Notes: BCa indicates bias-corrected and accelerated. *Significant point estimate (p-value < 0.05).
Abbreviations: Catastrophizing thoughts: Coping Strategies Questionnaire, Psychological distress: Hopkins Symptom Check List-25, Pain: Pain intensity (Numeric Rating Scale), Physical function: Subscale of RAND 36. Significant results in bold font.

association between high pain intensity and lower educational level among women, but more importantly, demonstrate that this association is partly mediated by catastrophizing thoughts (Table 8). A similar relation was established for the association between low physical function and lower educational level among women. This relationship was completely mediated by

catastrophizing thoughts (Table 8). Indeed, tendencies to catastrophizing thoughts in patients with chronic pain are well known,[42,44-48] and has been suggested to aggravate pain and hamper physical function.[47] Our findings indicate that the link between physical function and educational level among women with chronic pain was associated with catastrophizing

Table 11 Result of Reversed Mediation Model (The Significant Model from Table 10) with Pain as Mediator in Men, Based on 5000 Bootstrap Samples

	Independent Variable	Mediating Variable	Dependent Variable	Direct Effects	Indirect Effects	Bootstrapping BCa 95% CI	
						Lower	Upper
2.	Financial situation	Pain	Psychological distress	−0.3295*	−0.1076*	−0.2220	−0.0152

Notes: BCa indicates bias-corrected and accelerated, *Significant point estimate (p-value < 0.05).
Abbreviations: Hopkins Symptom Check List-25, Pain: Pain intensity (Numeric Rating Scale 0–10), Physical function: Subscale of RAND 36. Significant results in bold font.

thoughts. In general, negative health effects of negative cognitions like catastrophizing thoughts have been reported both for pain and other health problems[48,49] and in association with low socioeconomic status (SES).[23,24] Our results thus support and extend this line of research, indicating that catastrophizing thoughts may contribute to health problems among pain patients with low SES, in this study identified by educational level. However, in this cross-sectional study, we cannot conclude about the direction of any causality. The catastrophizing thoughts may lead to a reduced activity level, but could also be due to physical disability.

No mediating effects of catastrophizing thoughts were found among men, although men reported catastrophizing thoughts at a comparable level to women (Table 1). Thus, since women and men with chronic pain have comparable tendencies to catastrophizing thoughts, we may speculate whether these cognitions contribute to perceived health problems among lower educated women but not men, suggesting that women are more vulnerable to these mechanisms than men. Perceived poor financial situation is another SES factor that our results confirmed to be associated with the patients´ health problems. Both women and men with a perceived poor financial situation reported relatively higher pain intensity. However, for both genders, the mediation analyses revealed that these relations were fully explained by psychological distress. It should be noted that our study reports perceived financial situation, and not the patient's income level. We were not seeking an objective measure of SES, but the subjective appraisal of the financial situation. This taps into the stress component of the concept of economic hardship, as discussed by Rios and Zautra.[50] Our findings further suggest that the link between stress related to their personal economy and pain intensity is mediated by a psychological distress. Although other studies have correspondingly found a relation between both poor financial situation and low educational level and pain-related outcomes.,[25,26] a causality remains to be confirmed with a prospective study design.

The biopsychosocial model of pain is complex. It involves the interaction of multiple factors, and bidirectional relations between biological, psychological and social factors.[51] The reversed models in this study confirm this assumption. One of the reversed models (Model 2, Table 9) showed a relatively stronger, mediating effect of pain intensity on catastrophizing thoughts among women with low education than the hypothesized model (Table 8), where catastrophizing thoughts were mediator. This may suggest that pain intensity triggers catastrophizing thoughts in lower educated women (Table 9). In men, however, the indirect effect of perceived financial situation on psychological distress in the reversed model (Table 11) was only partly mediated by pain intensity, while psychological distress as mediator in the hypothesized model showed a relatively stronger effect (Table 10). This could indicate that psychological distress in a setting of perceived poor financial situation may aggravate the pain intensity in men.

In our study sample and in line with previous studies[27,52] the psychological factors catastrophizing thoughts and psychological distress accounted better for pain problems for both genders than demographic factors. For both genders, there were moderate to strong bivariate relations between pain intensity and physical function, and between psychological distress and catastrophizing. These findings have been well established in a range of studies[45,53,54] and may reflect that chronic pain causes suffering for both genders.

An important contribution of this study is the detection of mediating factors in the well-established associations between demographic and psychological factors, pain and physical function. Separate analyses for men and women indicated some gender-specific mediators in these relations, but further studies are needed to establish whether there are any significant gender differences.

Limitations and strengths
We investigated psychological and demographic variables based on already known associations with pain and

physical functions, but limited by a cross-sectional design we could not conclude on potential causal relations between the investigated variables. Other variables, not included in our analyses, might also contribute to the relationships presented in this paper. The study sample further represents a highly selected sample of patients referred and admitted to a pain clinic, and may not be representative for the population of chronic pain patients in general. Furthermore, a majority of the patients referred to our pain clinic are women, and we cannot rule out gender or other biases in the referral practice by GPs and referring hospitals.

The questionnaire was primarily compiled for clinical use and some categorical questions concerning work, education and perceived financial situation were not validated. However, the HSCL-25, RAND-36, NRS, 2-items from CSQ are validated and frequently used in clinical research.

A strength of the study is the inclusion of a complete population admitted to a multidisciplinary pain clinic within a given time frame representing the most complex cases, which increases the generalizability for patients referred to multidisciplinary pain clinics.

The methodological approach, testing potential mediations, further provides new insights to the complex relation between factors associated with pain and physical function in patients with chronic pain. With this insight, we can establish new hypotheses on causality for future research on more individualized and gender-specific treatment programs.

Conclusion

This study identified mediating psychological variables associated with pain intensity and physical function. This may have important clinical implications, directing clinicians' awareness to the complex relationships of demographics and psychological factors mediating chronic pain and physical function, and suggesting a more gender-specific, multidisciplinary approach in the treatment of chronic pain. The findings also imply the need for further research on this topic.

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Disclosure

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