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Risk factors predicting the development of widespread pain from chronic back or neck pain

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Abstract

Emerging evidence suggests that some individuals with regional pain disorders go on to develop chronic widespread pain (CWP). However, the mechanism behind this transition and nature of risk factors that predispose a person to develop CWP remain to be elucidated. The purpose of this study was to describe the frequency with which participants with chronic back or neck pain develop CWP and to determine the risk factors associated with this development. In a sample of 512 individuals, we found that nearly a quarter (22.6%) of subjects who presented with regional back or neck pain in 2001/2002 had developed CWP by 2007. Logistic regression indicated that seven factors were associated with the transition to CWP: moderate or severe pain intensity, female gender, history of abuse, family history of CWP, severe interference with general activity, having one or more central sensitivity syndromes, and using more pain management strategies. History of abuse was not significant in multivariate analysis. Notably number of depressive symptoms endorsed, pain duration, age, body mass index, number of medication classes used, and receipt of disability benefits were not significantly associated with this transition.

Keywords

Widespread pain; spinal pain; fibromyalgia; risk factors

Introduction

Emerging evidence suggests that a subset of individuals with regional pain progress to the development of widespread pain. Studies investigating this transition report that 10.4% to 17.4% of patients with various regional pain sites develop chronic widespread pain (CWP).^{3,19-41} One study investigating the presence of CWP specifically in individuals with low

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Perspective: This study offers insight into risk factors associated the development of CWP. This information not only offers clues as to the mechanism behind the expansion of pain sensitivity from a regional pain locus to a widespread pain disorder but also provides insight as to how clinicians might mitigate this transition.

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back pain found that 24.5% of patients developed CWP over an 18 year period.³⁰ In subjects with chronic neck pain or post whiplash injury, some 10% to 22% have been found to develop CWP or FM.^{2,5,25} While it is clear that regional pain can progress to CWP in some instances, the mechanism behind this transition and the nature of risk factors that predispose a person to this transition remain to be elucidated.

Previous work investigating risk factors for the development of CWP and FM has largely focused on individuals following a whiplash injury or used population based studies involving individuals with non-specific single site pain. Risk factors for the development of CWP and FM post whiplash have included injury related factors such as perceived severity of the trauma and pain^{5,25,49}, number of pain sites and self assessed depression following the accident.²⁵ Studies examining new onset CWP in individuals with no pain or a mix of regional pain disorders have found risk factors to include age and family history³, longer lasting pain and self assessed depression¹⁹, and the presence of somatic symptoms and increased illness behavior.^{24,32} Although Forseth and colleagues¹⁹ found the presence of low back pain to be a specific predictor for developing FM, only one group has studied the development of CWP or FM specifically in patients with low back pain.³⁰ This latter group reported that 25% of patients with back pain developed FM over an 18 year period, and that being female or having a postural disorder were significant predictors of this transition.

The current study set out to add to this previous research by specifically investigating the development of CWP in individuals with chronic low back and neck pain. This particular population was chosen due to the emerging evidence suggesting that a subset of individuals with these disorders develop central sensitization as evidenced by widespread hyperalgesia to various painful stimuli^{9,26,39} and recent imaging studies showing enhanced activation of pain related areas in the brain in response to mildly painful stimuli.^{16,22} Central sensitization can predispose an individual to widely disseminated pain when repetitive tonic input from a localized source of pain produces an expansion of receptive fields, such that pain perception expands beyond the initial locus to involve a larger region.^{17,46} The development of central sensitization in some individuals with chronic low back or neck pain might place them at greater risk for a transition to CWP. The current study aimed to describe the development of CWP in patients who had presented some six years previously with back or neck pain and to determine the risk factors associated with this transition. Preliminary results of this study were presented at the 2009 American Pain Society Scientific Meeting.²⁸

Methods

Subjects and study design

This was a retrospective cohort study of patients who had been seen at a local pain clinic with a diagnosis of chronic low back or neck pain. Individuals were identified as potential study subjects through a search of electronic medical records of patients 21 and older, seen by the pain clinic during 2001 and 2002. Visit diagnoses, assigned by the pain clinic physician at the time of the initial consultation, were reviewed to identify patients seen for one of 25 diagnoses representative of back or neck pain. Examples of included diagnoses were spondylosis of cervical or lumbar joint, spondylolisthesis of cervical or lumbar joint, cervical or lumbar spinal stenosis, cervical or lumbar radiculopathy, low back pain, cervicgia and other related diagnoses. This gave us a sampling frame of 2,256 potential study participants. In 2007 these 2,256 patients were invited to participate in the current research study. Subjects choosing to participate provided informed consent following guidelines set forth by the Kaiser Permanente Center for Health Research's Institutional Review Board. Upon first seeing the pain clinic in 2001/2002, patients completed a questionnaire which contained a body drawing for marking pain locations and questions regarding various dimensions of pain and related symptoms. In 2007, subjects agreeing to

participate in the current study were sent a study survey containing a body drawing and follow up questions regarding their current pain. Body drawings completed in 2001/2002 were compared to the body drawings completed in 2007 to determine the proportion of participants who had regional back or neck pain in 2001/2002 and developed CWP by 2007. Data on the 2001/2002 clinical questionnaire and data retrieved through a retrospective chart review were used to determine which variables preceded, and therefore might predict, the development of CWP.

Questionnaires

In 2001 or 2002, patients completed a clinical questionnaire prior to being seen by the pain clinic. This questionnaire included two line drawings of the body (front and back) on which patients were asked to shade the sites where they experienced pain. The distribution of pain on this manikin was used to determine the presence of CWP according to the 1990 American College of Rheumatology (ACR) Fibromyalgia Classification Criteria.⁴⁸ Thus a diagnosis of CWP was made if a participant presented with pain in three out of four body quadrants including axial pain. Determination of pain status (regional versus widespread) was made by one author (LLK) with questionable body drawings referred to two researchers with extensive experience diagnosing CWP and FM (KDJ and RMB). Participants deemed to have CWP in 2001/2002 were excluded from analysis, as the study was investigating a transition to CWP from chronic regional pain in the low back or neck. The clinical questionnaire completed in 2001/2002 also gathered data on clinical characteristics such as pain severity (measured on a 0-10 numerical rating scale (NRS)), pain interference with general activity and sleep (measured on a 0-10 NRS), pain duration (number of years in pain), body mass index (BMI), history of abuse as a child or adult, number of back or neck surgeries, number of depressive symptoms (out of the nine depressive symptoms listed in the Personal Health Questionnaire (PHQ 9) and use of tobacco. Patients were also asked to indicate the pain management strategies they had utilized in the past. The questionnaire listed 14 commonly used pain management strategies including behavioral (relaxation, pacing), activity oriented (walking, swimming, yoga), cognitive (therapy, meditation), complementary (acupuncture, chiropractic, massage) and traditional (steroid injections, medicated lotions, TENS unit) therapies. For purposes of data analysis, this information was collapsed to reflect the total number of pain management strategies used by participants with a range of zero to 14. Demographic information was collected from this questionnaire including age, gender, work status, and receipt of disability benefits. Given that the purpose of the 2001/2002 questionnaire was to gather data to inform clinical treatment, the wording of two important questions had not been validated for research. In assessing the patient's level of depression, the clinical questionnaire used the text from the PHQ 9 but not the scoring method validated for research. Patients were asked to indicate which depressive symptoms they had experienced in the past two weeks instead of rating the severity of these symptoms as indicated in the validated version of the PHQ 9.²⁹ Information regarding history of abuse was gathered by simply asking patients to answer yes or no as to whether they had been abused as an adult or child.

Participants who had agreed to participate in the current study were sent a questionnaire in 2007. This questionnaire included two line drawings of the body (front and back) in which the participants again shaded in the sites where they currently experienced pain. This information was used to determine the presence of CWP in 2007 according to the ACR diagnostic criteria (i.e. axial pain plus pain in three or more body quadrants).⁴⁸ Participants found to have CWP in 2007 had, by study definition, transitioned from regional back or neck pain in 2001/2002 to CWP during the period of 2001/2002 to 2007. The study questionnaire completed in 2007 gathered data on participants' current pain and clinical status. The 2007 study questionnaire also collected information on family history of CWP

and the presence of comorbid conditions that have presented with evidence of central sensitization in past studies including irritable bowel syndrome 45-47, irritable bladder syndrome 38-44, migraines 4,11, and restless legs.⁴³ Participants were asked to identify the year in which they were diagnosed with these comorbidities. Instances where onset of these syndromes occurred subsequent to 2002 were not included in analyses in an attempt to establish temporal precedence between the onset of these syndromes as compared to CWP. Although presence of these comorbidities indicates pain in an area other than the back or neck, we relied on the patient's body drawing for determination of regional versus widespread pain, a method extensively used in this type of research.^{24,34} Finally, in order to discover the impact of medication on the development of CWP, a retrospective chart review was done to gather data on medication used by the participants in 2001/2002. The six month period surrounding the participant's visit to the pain clinic in 2001/2002 was reviewed and use of the following medication classes were documented: long acting opioids, short acting opioids, non-steroidal anti-inflammatories, oral steroids, anticonvulsants, tricyclic antidepressants, selective serotonin reuptake inhibitors, serotonin and norepinephrine reuptake inhibitors, muscle relaxants, benzodiazepines, sleep medications and topical analgesics. For data analysis, this information was collapsed to reflect the total number of medication classes used during the specified time period for a range of zero to twelve.

Statistical analysis

Those subjects who presented with regional back or neck pain in 2001/2002 and completed the 2007 study questionnaire were included in the analysis. The bivariate associations between developing CWP during the time period between 2001/2002 and 2007 and the potential risk factors were estimated using logistic regression analyses. To enhance the clinical relevance of logistic regression, some continuous variables were transformed into categorical variables based on theoretically supported cutoffs as described below. This allowed interpretation of the parameters from logistic regression to reflect clinically meaningful units of change. Pain severity and interference were categorized into mild pain (0 to 4 out of 10), moderate pain (5 to 7 out of 10) and severe pain (8 to 10 out of 10). This categorization was based on a recent nationwide, population based study.⁴⁰ BMI was transformed into normal weight (24.9 kg/m² and below), overweight (25 to 29.9 kg/m²) and obese (30 kg/m² and above) according to Center for Disease Control guidelines. Based on the distribution of the number of pain management strategies used in 2001/2002, this variable was transformed into a categorical variable with each unit representing an increase of three strategies used. Age was reclassified into the categories outlined by the Centers for Disease Control. However, based on the distribution in the sample, only the categories of 44 years and younger, 45 to 64 years and 65 years and older were used. Odds ratios obtained through the logistic regression analyses were converted to relative risks using the procedures suggested by Zhang and Yu.⁵¹ Therefore the results are presented as odds ratios and relative risks with associated 95% confidence intervals (CI) and p values. Risk factors found in the bivariate analyses to be associated with the development of CWP were entered into a multivariate logistic regression model to determine the relative predictive value of each risk factor while controlling for the other risk factors. Results of the multivariate analysis are presented as odds ratios with associated 95% CIs and p values. All analyses were performed using SPSS for Windows, Version 15.0 (SPSS Inc., Chicago Illinois).

Results

A total of 550 subjects (24.4% response rate) seen by the local pain clinic in 2001/2002, completed and returned the 2007 study questionnaire. On examination of the subjects' 2001/2002 body diagram, 38 (6.9%) subjects met criteria for CWP in 2001/2002 and were therefore excluded from analysis. Demographics for the remaining 512 participants are

presented in Table 1. The body diagrams of the 512 subjects revealed that 432 presented with back pain while 80 subjects indicated having neck pain in 2001/2002. Statistical analysis (t-test and X^2) comparing individuals with back pain to subjects with neck pain indicated that individuals with back pain were significantly older (mean age 65 years, SD 14 years) as compared to those with neck pain (mean age 59 years, SD 12 years), $t_{(470)}=2.772$, $p=.001$. Further analysis revealed no differences between the two groups on gender ($p=.355$), pain duration ($p=.112$), pain intensity ($p=.195$), BMI ($p=.503$), depressive symptoms ($p=.701$) or total number of medication classes prescribed ($p=.362$). Since the two groups did not differ on pain related variables, the subjects were combined into one group for the remaining analyses. A review of the participants' 2007 body drawings indicated that 114 (22.6%) had CWP and therefore had transitioned from regional back or neck pain in 2001/2002 to CWP by 2007. Table 2 compares the group who presented with CWP in 2007 to the group who continued to have regional pain on variables thought to be potential risk factors for the development of CWP. Using logistic regression, we assessed which of these variables were associated with a transition to CWP. Table 3 shows the bivariate associations among the risk factors of interest and the development of CWP. Subjects who presented with severe pain in 2001/2002, as compared to having mild pain, were nearly five times more likely to develop CWP whereas those participants who had moderate pain in 2001/2002 were more than three times more likely to develop CWP over the six year study period. Subjects having severe pain interference with general activity in 2001/2002, as compared to mild interference, were twice as likely to develop CWP. Using more pain management strategies in 2001/2002 was associated with a 46% increased likelihood of developing CWP. Females were more than twice as likely to develop CWP as were subjects who had a female family member with CWP. Participants who had a history of abuse as an adult were two and a half times more likely to develop CWP whereas having a history of abuse as a child increased the likelihood of developing CWP by 73%. Subjects with two or more painful comorbidities (irritable bowel syndrome, irritable bladder syndrome, restless legs syndrome, and/or migraines) were nearly three times more likely to develop CWP as compared to those participants with no comorbidities. Clinical features reported in 2001/2002 that were not significantly associated with the development of CWP were: the participant's age, pain duration, pain region (back or neck), number of depressive symptoms endorsed by the participant, number of back or neck surgeries prior to 2001, BMI, number of medication classes used for pain management in 2001/2002, tobacco use history, and receipt of disability benefits. It is worthy of note that the number of depressive symptoms endorsed in 2001/2002 and having an obese BMI in 2001/2002 did trend towards significance (.089 and .080, respectively).

Risk factors that were significantly associated with the development of CWP were entered into a multivariable logistic regression model to determine which variables predicted a transition to CWP when controlling for all other variables. When appropriate, only one variable was included to represent a similar set of risk factors. Therefore the multivariable analysis included pain severity, family history of a first degree relative(s) with CWP, gender, number of pain management strategies used in 2001, number of painful comorbidities, and history of abuse. The results of this analysis are displayed in Table 4; it is seen that all risk factors remained significant except the history of abuse (adult and childhood). Having a history of abuse was significantly correlated with three of the other risk factors including gender ($r=.191$, $p=.01$), number of pain management strategies used ($r=.154$, $p=.01$), and having a painful comorbidity (irritable bowel syndrome, irritable bladder syndrome, restless legs syndrome, and/or migraines) ($r=.093$, $p=.05$).

Discussion

This study examined the frequency with which participants with chronic low back or neck pain developed chronic widespread pain (CWP) over the course of some six years and attempted to discern the risk factors associated with this transition. Nearly a quarter (22.6%) of subjects who presented with regional back or neck pain in 2001/2002 had developed CWP by 2007. The transition to CWP in this cohort of individuals is higher than previous studies that have examined the development of CWP in individuals with a mix of regional pain disorders. For instance, the development of CWP among individuals with regional pain at any location has been reported at 10.4%⁴¹, 16.4%³, and 17.4%¹⁹, whereas the development of CWP in individuals with chronic low back or neck pain has been reported at 24.5%³⁰ and 21%²⁵. Taken together with research identifying central sensitization as a common underlying mechanism in some patients with chronic low back or neck pain and most patients with CWP, it is reasonable to speculate that individuals with regional pain in the spine have a greater propensity for the development of CWP as compared to patients with other peripheral pain syndromes. Although this hypothesis has yet to be substantiated, one study comparing patients with chronic low back pain to those with chronic muscle tension headaches found that individuals with spinal pain displayed enhanced cortical activation to noxious stimuli, decreased habituation to multiple stimuli, and greater sensitization to painful stimulation.¹⁸ More profound neuroplastic changes in the central nervous system, as a result of pain in the spine, could explain the higher frequency of CWP development in patients with axial disorders.

Seven factors were individually associated with the development of CWP from chronic low back or neck pain: moderate or severe pain intensity, female gender, history of abuse, family history of CWP, severe interference with general activity, having one or more painful comorbidity (irritable bowel syndrome, irritable bladder syndrome, restless legs syndrome, and/or migraines), and using more pain management strategies. Notably number of depressive symptoms endorsed by the subject, pain duration, age, BMI, number of medication classes used, and receipt of disability benefits were not associated with this transition, although number of depressive symptoms and being obese trended toward significance. In comparison to increased pain severity having relative risk of nearly five, other risk factors were relatively modest. The strong predictive nature of intense pain is comparable to findings from other studies that have investigated the development of CWP from regional pain.^{25,37} Contemporary research supports the notion that persistent high intensity nociceptive input can augment neuroplastic changes in the central nervous system and lead to expansion of receptive fields and more widespread symptomatology.¹⁶

Consistent with research demonstrating that CWP disproportionately affects women^{8,23,36}, this study found that being female was a significant risk factor for the development of CWP. A recent, comprehensive review of sex differences in clinical and experimental pain concluded that women and men process pain differently, perhaps contributing to the over representation of women in some, but not all, disorders of pain processing.¹³ For instance, temporal summation is greater in females¹⁴, imaging studies have demonstrated augmented central processing of nociception in females, and males have demonstrated more efficient diffuse noxious inhibitory control (DNIC) as compared to females in some studies.^{21,42} Differential processing of ongoing pain between men and women, particularly related to enhanced facilitation and impaired inhibition, could provide physiological rationale for more frequent development of CWP in females.

The finding that a family history of CWP significantly predicted the development of CWP provides added support to genetic and familial influences affecting individual differences in pain susceptibility. Individuals with FM (of which CWP is the hallmark symptom) have

single nucleotide polymorphisms (SNPs) in the serotonin, dopamine, and catecholamine systems which affect pain processing in this syndrome.¹⁵ Specifically, patients with FM have been found to have a variant allele in the COMT gene which codes for Catechol-*O*-methyl transferase; this enzyme degrades epinephrine, nor-epinephrine and dopamine, all monoamines involved in pain processing. Other studies have reported SNPs in the serotonin transporter gene and serotonin receptor subunits which may explain the diminished DNIC of patients with FM.^{10,20} Since the current study did not collect DNA samples, the finding of familial aggregation of CWP still cannot address the relative contribution of genetics versus environmental influences in the development of chronic pain.

An intriguing finding from this study was the observation that having a comorbid pain syndrome (irritable bowel syndrome, irritable bladder syndrome, restless legs syndrome, and/or migraines) was associated with the development of CWP; in fact having more than one of these syndromes was associated with a substantially increased risk of developing CWP. Contemporary research into these particular disorders suggests that they are characterized by dysregulation in peripheral and central nervous system pathways leading to enhanced pain perception.¹² While the co-occurrence of disorders with evidence of central sensitization has been relatively well established¹⁷, the influence of having one syndrome on the development of another such syndrome has not been well characterized. The current study provides some initial evidence that individuals with one or more of these syndromes have an increased propensity to develop another disorder characterized by pain processing abnormalities. This finding adds support to the previously proposed notion⁵⁰ that a similar underlying pathophysiological mechanism, namely central sensitization, might unite these disorders.

Several limitations could impact the interpretation of this study. Although we know that participants did not have CWP or a history of FM in 2001/2002 and that a subset of individuals did have CWP in 2007, we do not know the precise progression of pain during this six year period; thus we are unable to calculate the rate of transition to CWP. There is also a remote possibility that some individuals had CWP prior to 2001 but had a remission of widespread pain during their pain clinic assessment in 2001/2002. However, most studies and general clinical experience indicate that the majority of individuals with CWP at baseline continue to meet diagnostic criteria for widespread pain at follow up.^{27,31,34} A similar limitation relates to not having a firmly established timing of disease onset in regards to CWP and comorbidities characterized by central sensitization. Although participants were asked to report year of diagnosis, retrospective recall of this information cannot be considered entirely reliable. Not knowing precise onset of these conditions precludes any indication of causation or consequence and only indicates an association between these disorders.

Other limitations involved the use a questionnaire designed for clinical purposes to gather data from 2001/2002. While this method allowed for a six year follow up without the time and costs associated with a six year prospective study, the 2001/2002 questionnaire did not use wording validated for research in the collection of two important variables. This could be one explanation why depression was not found to be a significant risk factor in the current study despite somewhat consistent research findings that psychological distress often precedes the development of CWP and FM.^{19,24,25} Studies identifying this association have used validated measures which produce a score associated with the level of psychological distress experienced by the participant.^{24,33} Merely endorsing the presence or absence of certain depressive symptoms might not have allowed for adequate variability or an accurate assessment of depression in this study's subjects. The method for collecting abuse history could have been similarly problematic. Recent research⁶ into this phenomenon suggests that using a structured interview that asks about specific events that would constitute physical or

sexual abuse can avoid recall bias and what some researchers have termed “effort after meaning”.³⁵ Without identifying specific events, subjects looking to find an explanation for their symptoms might more frequently define past experiences as abuse. Therefore, findings taken from asking about the broad concept of abuse, as was done in this study, must be interpreted with caution. Conclusions from this study are also limited by the relatively low response rate of 24.4%. Although the low response rate was likely due, in part, to individuals who had relocated or were no longer part of the healthcare system, a response bias towards individuals with more severe, continued pain cannot be excluded. Consent was not obtained from patients who did not respond to the study invitation and, therefore, their data could not be accessed to compare responders to non-responders.

In summary, this study advances the understanding of the relationship between chronic low back and neck pain and CWP and elucidates factors associated with the development of a widespread pain disorder. Understanding risk factors for the development of CWP should contribute insight into the mechanism behind the expansion of pain sensitivity from a regional locus to a widespread pain disorder and provide clues as to how clinicians might mitigate this transition. This is clearly an important goal as nearly a quarter of participants with regional back or neck pain developed CWP. The transition of CWP from pain in the back or neck could be a useful model to pinpoint the genetic and bio-psycho-social factors that are relevant to the development of fibromyalgia and similar syndromes.

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Table 1

Sample demographics

Demographic variable		n (%) or mean (SD)
Gender	Female	288 (56.3%)
	Male	223 (43.7%)
Ethnicity	Not Hispanic or Latino	384 (69.8%)
	Hispanic or Latino	9 (1.6%)
	Not reported	156 (28.6%)
Race	White	499 (90.7%)
	American Indian/Alaska Native and White	13 (2.4%)
	Black/African American	7 (1.3%)
	Asian	5 (0.9%)
	Native Hawaiian/Other Pacific Islander	2 (0.4%)
	American Indian/Alaska Native	1 (0.2%)
	Not reported	23 (4.2%)
Age in 2001/2002		57.7 (13.7)
Employment status in 2001/2002	Full time	165 (32.2%)
	Part time	61 (11.9%)
	Work from home	33 (6.4%)
	Retired	160 (31.3%)
	Unable to work due to pain	20 (3.9%)
	Not reported	73 (14.3%)
Disability benefits in 2001/2002	Not receiving disability benefits	338 (66.8%)
	Receiving disability due to pain	74 (15.1%)
	Receiving disability unrelated to pain	78 (15.1%)
Pain location In 2001/2002	Back	432 (84.4%)
	Neck	80 (15.6%)
Duration of pain in 2001/2002	Within one year	53 (10.4%)
	One to two years	198 (38.7%)
	Three to four years	74 (14.5%)
	Five or more years	109 (21.3%)
	Not reported	78 (15.2%)
Pain severity in 2001/2002	Mild	258 (50.4%)
	Moderate	213 (41.6%)
	Severe	39 (7.6%)
Pain interference with activity in 2001/2002	Mild	88 (24.4%)
	Moderate	174 (48.2%)
	Severe	99 (27.4%)

Demographic variable	n (%) or mean (SD)	
BMI in 2001/2002	Normal	106 (23.6%)
	Overweight	171 (38.0%)
	Obese	148 (32.9%)
	Morbidly obese	25 (5.6%)

Table 2

Comparing individuals who developed CWP by 2007 to those who did not on potential risk factors.

Risk factor	CWP (mean (SD) or % positive) n = 114	No CWP (mean (SD) or % positive) n = 398
Pain severity (2001/2002) (range 0-10)	6.1 (1.8)	5.6 (1.9)
Female gender	76.3%	50.6%
Abused as an adult (2001/2002)	16.5%	3.6%
Pain interference with general activity (2001/2002) (range 0-10)	6.5 (2.1)	5.8 (2.4)
Number of pain management strategies used (2001/2002) (range 0-14)	8.1 (3.6)	6.2 (3.5)
First degree relative with CWP	63%	41.4%
Female family member with CWP	64.7%	38.1%
Elder family member with CWP	59.4%	37.5%
Sibling with CWP	48.9%	23.9%
History of irritable bowel syndrome	37.7%	18.6%
History of irritable bladder syndrome	18.4%	7.5%
History of restless legs	23.7%	12.1%
History of migraines	28.9%	18.3%
Total number of painful comorbidities (range 0-4)	1.1 (1.0)	0.6 (0.7)
Age (range 22 – 97 years)	62.5 (14.3)	64.2 (13.8)
Pain duration (years) (2001/2002) (range 11 months - 32 years)	9.5 (4.6)	10.2 (5.6)
BMI (2001/2002) (range 17.9 – 70.9)	30.6 (8.0)	28.9 (5.5)
Number of back or neck surgeries prior to 2001	0.5 (0.8)	0.5 (0.7)
Number of depressive symptoms endorsed (2001/2002) (range 0-9)	3.0 (2.2)	2.6 (2.1)
Number of medication classes used for pain (2001/2002) (range 0-12)	2.6 (1.7)	2.3 (1.5)
Tobacco pack year history (2001/2002) (range 1 - 80)	15.7 (21.9)	12.9 (18.9)
Receipt of disability benefits (2001/2002)	19.4%	19.2%

Table 3

Bivariate risk factors associated with the development of CWP from regional back or neck pain.

Risk factor	Odds ratio	Relative risk	RR 95% CI	Significance
Pain severity in 2001/2002 (mild pain referent)				
Pain severity (severe pain vs mild pain)	9.81	4.94	2.7 - 7.4	p<.001
Pain severity (moderate vs mild pain)	4.47	3.22	4.6 - 20.8	p<.001
Female gender	3.14	2.35	1.9 - 5.1	p<.001
Abused at anytime in life	2.65	2.016	1.6 - 2.7	p<.001
Pain interference with general activity in 2001/2002 (severe vs mild interference)	2.41	1.95	1.2 - 4.9	p=.015
More pain management strategies in 2001/2002	1.50	1.46*	1.3 - 1.8	p<.001
First degree relative with CWP	2.41	1.90	1.5 - 3.8	p<.001
Female family member with CWP	2.98	2.20	1.9 - 4.7	p<.001
Elder family member with CWP	2.43	1.9	1.5 - 3.9	p<.001
Sibling with CWP	3.05	2.19	1.9 - 4.9	p<.001
History of irritable bowel syndrome	2.65	2.04	1.7 - 4.2	p<.001
History of irritable bladder syndrome	2.77	2.05	1.5 - 5.1	p=.001
History of restless legs	2.26	1.81	1.3 - 3.8	p=.002
History of migraines	1.81	1.56	1.1 - 2.9	p=.015
History of painful comorbidities				
One comorbidity vs none	2.19	1.88	1.3 - 3.6	p=.002
Two or more comorbidities vs none	3.96	2.79	2.3 - 6.9	p<.001
Age (44 years and younger referent)				
45 - 64 years	1.57	1.43	.6 - 4.0	.340
65 years and over	1.28	1.22	.5 - 3.2	.602
Pain location in 2001/2002				
Back pain	2.62	1.93	.3 - 21.0	.363
Neck pain	2.20	1.63	.3 - 19.1	.473
Pain duration (years in pain at 2001/2002)	.96	.94	.8 - 1.1	.586
BMI in 2001/2002 (normal referent)				
BMI (obese vs normal)	1.71	1.52	.76 - 2.4	p=.080
BMI (overweight vs normal)	1.31	1.24	.94 - 3.1	p=.391
Number of back or neck surgeries prior to 2001	1.12	1.09	.9 - 1.3	.439
Depressive symptoms in 2001/2002	1.10	1.08	1.0 - 1.2	.089
Number of medication classes used for pain in 2001/2002	1.10	1.08	1.0 - 1.3	.147
Tobacco pack year history in 2001/2002	1.01	1.01	1.0 - 1.0	.224
Receipt of disability benefits in 2001/2002	1.01	1.01	.6 - 1.8	.968

* Relative risk calculated using dichotomized version of variable (use of zero pain management strategies versus one or more strategies used) whereas odds ratio calculated with the continuous variable.

Table 4

Multivariable analysis with all significant bivariate risk factors

Risk factor	Odds ratio	Significance	95% CI
Pain severity in 2001/2002	3.92	p<.001	2.6 – 6.0
Family history of CWP	1.92	p=.013	1.2 – 3.2
Gender	2.32	p=.003	1.3 – 4.1
Number of pain management strategies used in 2001	1.29	p=.016	1.1 – 1.6
History of having two or more painful comorbidity vs having no comorbidities	2.01	p=.039	1.0 – 3.9
History of having one painful comorbidity vs having no comorbidities	1.05	p=.883	.6 – 1.9
History of abuse in lifetime	1.49	p=.221	.8 – 2.8