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Heterogeneous depression responses to chronic pain onset among middle-aged adults: A prospective study



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ABSTRACT

Studies on depression response to chronic pain are limited by lack of clarification of different forms of response patterns and cross-sectional measures. The current study examined heterogeneous long-term patterns of depression response to chronic pain onset prospectively using the mixture modeling technique. Depression symptoms prior to and following pain onset over a course of six years were charted in a nationally representative middle-aged sample. Four distinct depression symptom trajectories emerged. The *resilience* (72.0%) trajectory describes a pattern of no/minimal depression symptoms prior to and following pain onset. The *post-pain depression* trajectory (11.4%) describes a pattern of low depression at baseline and increasing symptoms following pain onset. The *chronic depression* (6.8%) trajectory is characterized by persistently high depression symptoms irrespective of pain onset. The *prior depression improved* (9.8%) trajectory describes a pattern of high depression at baseline and gradually declining symptoms following pain onset. Self-rated health at both baseline and following pain onset predicted the *resilience* trajectory. Baseline self-rated health distinguished the *post-pain depression* and *chronic depression* trajectories. Individuals in the *prior depression improved* trajectory were older and had more chronic illnesses at baseline but fewer illnesses following pain onset, compared to those in the *resilience* or *post-pain depression* trajectory.

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1. Introduction

Chronic pain is a prevalent and potentially debilitating health condition. In the United States, it is estimated that more than one-third of the population are living with chronic pain (Institute of Medicine, 2011), and pain-related complaints are one of the leading causes for physician visits (Gatchel, 2004). Pain experiences are aversive and noxious, and adjustment to pain typically involves prolonged treatments and rehabilitation programs which effectiveness are yet to be proven (Turk et al., 2011). Given the challenges facing individuals with chronic pain, it is not surprising that heightened rates of psychological dysfunction are found in this population (Dersh et al., 2002). In particular, a substantial body of research has documented higher prevalence rates of depression among pain patients (Bair et al., 2003; Sharp and Keefe, 2005; Tunks et al., 2008) than those among other medical populations (Livingston et al., 2000).

Studies on depression response to pain have almost exclusively focused on the detection of depression at one time point, based on a predetermined set of criteria or score defining the mental

disorder. This body of research has laid important groundwork for the understanding of the prevalence, as well as risk factors, of depression outcome to pain. There are, however, several limitations to this approach. First, predefined categories of presence or absence of depression depend heavily on assessment methods and theoretical grounding, which may vary across studies, leading to inconsistent results. Moreover, dichotomous division of depression versus non-depression may obscure other meaningful response patterns to pain experiences (Bonanno, 2004; Bonanno et al., 2011). In particular, individuals with few or no depression symptoms, typically being grouped into the same category as those who show sub-threshold depression, may in fact represent a pattern of healthy adjustment, and investigation of this form of response could lead to insights into protective factors against the development of depression to pain.

Although not specifically focused on depression response, a line of research has started to investigate the nature and prevalence of healthy, or resilient adjustment, to pain (Strugeon and Zautra, 2010; Yeung et al., 2012; Karoly and Ruehlman, 2006). Karoly and Ruehlman (2006) identified a group of “pain resilience” individuals, defined as low emotional distress and low pain-related functional interference in the presence of high chronic pain severity. They found that the pain resilience group demonstrated higher task persistence, less pain-related fear, less catastrophizing

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Table 1
Demographic summary of the sample.

	N	Percentage (%)		N	Percentage
Gender			Marital status		
Male	717	33.0	Married	1549	71.3
Female	1455	67.0	Divorced/separated/widowed	510	23.5
Missing	0	0.0	Never married	86	4.0
Race/Ethnicity			Missing	27	1.2
White	1520	70.0	Employment		
Black	349	16.1	Employed	1281	59.0
Hispanic	257	11.8	Unemployed	601	27.7
Others	46	2.1	Retired	268	12.3
Missing	0	0.0	Missing	22	1.0
Education			Household income		
High school or below	1364	62.0	< \$10,000	272	12.5
College or some college	644	29.7	\$10,000 – \$100,000	1617	74.4
Graduate or professional school	177	8.1	> \$100,000	281	12.9
Missing	5	0.2	Missing	2	0.1

thoughts, and less dependence on health care support than a demographically matched non-resilience group. The study provides initial evidence that healthy adjustment (i.e., low depression) is a legitimate form of psychological response to pain, and suggests several possible protective factors that may buffer the impact of pain experiences. Nevertheless, as in depression and pain research, studies on “pain resilience” also rely on theoretical conceptualization for group designation, and are therefore subject to artificial division of groups.

Another limitation of the existing studies is the paucity of longitudinal data on the course of depression among pain patients, especially measures on pre-pain depression symptoms. Several studies have reported an increased risk of persistent depression for those who have elevated depressive symptoms prior to pain onset (Katon et al., 1994; Magni et al., 1994). Investigation of pre-morbid depression is made more important as this form of depression response may be informed by risk factors that are different from those associated with depression developed in reaction to pain.

Concurrence of pain and depression is associated with more pain symptoms, higher pain intensity, longer pain duration, as well as higher rates of disability and health care utilization, in comparison to pain condition alone (Bair et al., 2003; Arnow et al., 2006). The greater burden imposed by the comorbidity on both the patients and health care system calls for more systematic and refined investigation of depression responses among individuals who suffer from chronic pain. The current study utilized a recently developed statistical approach, Latent Growth Mixture Modeling (LGMM), to prospectively chart longitudinal depression trajectories to pain onset among a nationally representative sample over the course of six years. The mixture modeling technique maps longitudinal response patterns based primarily on the intrinsic properties of the data structure (Muthén, 2004), which largely overcomes the limitation of priori assumptions in group assignment. It has been suggested that the middle-aged population is at particularly high risk of psychological dysfunction following pain, and that psychosocial mediators of pain-depression association might be age specific (López-López et al., 2008). Hence the ages of the sample were limited to 45–65 years old, in order to minimize the impact of age on the trajectories.

We also investigated predictors that could differentiate depression trajectories. Based on previous research on pain and depression comorbidity, three health-related predictors, namely pain-induced functional impairment, chronic illness and perceived health, were selected. Studies using a variety of pain samples and assessment methods have consistently suggested pain-induced functional

impairment to be robustly associated with comorbidity of pain and depression (Bair et al., 2003). In a global study of pain patients in primary care from 14 countries, impairment to daily activities emerged as the strongest predictor of depression or anxiety (Gureje et al., 2001). We also assessed the number of other concurrent medical conditions, as their presence may increase the risk of depression among chronic pain patients (Ohayon and Schatzberg, 2003). On the other hand, subjective perception of health status could contribute significantly to the development of depression, above and beyond pain-related complaints and other medical conditions (Carroll et al., 2003). We included both pre- and post-pain measures of medical illness and perceived health for their possible differential effects on the trajectories (Gatchel, 2004). Finally, the predictive values of a wide range of demographic variables, including age, gender, marital status, employment status, household income and ethnicity, were also examined.

2. Method

2.1. Study background

Data were obtained from the public release of the Health and Retirement Study (HRS, University of Michigan). The HRS is a longitudinal, nationally representative study surveying older Americans and their spouses once every two years on various mental and physical health-related aspects between 1992 and 2010. Overall response rates ranged from 80.4% to 89.4% across the survey years.

2.2. Subjects

To ensure that each subject had one Baseline (BL) and at least three measured time points following pain onset (T1, T2, T3), a floating baseline method was used. Subjects who reported moderate or severe pain in any wave between 1996¹ and 2006 (T1) and no pain in the immediate previous wave (BL) were selected. The ages of the subjects were limited to between 45 and 65. This resulted in a total of 2453 individuals. In order to improve the accuracy of initial depression response to pain onset, subjects who had no valid depression scores at either BL or T1 were excluded from the study, giving a final sample of 2172 individuals (73.2% with moderate pain and 26.8% severe pain). The demographic characteristics of the sample are summarized in Table 1. Eighty six percent of the sample had depression measures at all four time points, and 91% had depression measures at three time points. The excluded cases ($N=281$; 11.5%) comprised a slightly larger proportion of individuals with moderate pain (76.5%; $\chi^2=6.425$, $p<0.05$) than did the final sample. The two samples did not differ in pain-related functional impairment ($\chi^2=2.340$, $p>0.05$).

¹ The depression measure in 1992 comprised more items than the one used in subsequent years. To ensure consistency, data from 1992 was excluded in the study.

2.3. Measures

Subjects were asked various questions regarding their demographic information and health status in each wave. Measures of pain-related variables, perceived health and chronic illnesses were developed by the HRS Health Work Group, based on prior health survey literature and expert consultation (Fisher et al., 2005). Pain occurrence was assessed by the question “Are you often troubled with pain?” If a subject answered “yes” to the question, follow-up questions of “How bad is the pain most of the time? Is it mild, moderate or severe?” and “Does the pain make it difficult for you to do your usual activities such as household chores or work?” were asked to assess pain intensity and pain-induced functional impairment. Only subjects who reported moderate or severe pain were included in the analysis. Functional impairment was dummy coded into “1” (yes) or “0” (no). Perceived health was assessed by the question “Would you say your health is poor, fair, good, very good or excellent?” with responses coded from 1 (poor) to 5 (excellent). Presence of chronic illness was identified by the question “Has a doctor told you that you have (diabetes, heart conditions, hypertension, cancer, lung disease, stroke, arthritis)?” Total number of chronic illnesses was used in the current study (0–7).

Depressive symptoms were assessed by an abbreviated version of the Center for Epidemiologic Studies Depression scale (CES-D; Radloff, 1977), including eight items assessing sleep disturbance, energy level, motivation, effort in engaging in activities, and feelings of depression, sadness, happiness and loneliness, respectively. Total score was used for analysis (0–8). The CES-D scale has shown high reliability and validity in assessing depression in chronic pain populations (Geisser et al., 1997). The reliabilities of the abbreviated version of the CES-D scale ranged from 0.77 to 0.83 across the survey years (Steffick, 2000). A cutoff of four symptoms was recommended by the HRS for the assessment of clinically relevant depression (Steffick, 2000).

2.4. Data analysis

To identify heterogeneous growth trajectories of depression prior to and following the onset of pain, we tested one-to-five class unconditional latent growth mixture models using Mplus v6 (Muthén and Muthén, 2010). The LGMM method combines techniques of the traditional Latent Group Analysis (LCA) and growth curve modeling by simultaneously capturing meaningful groups of individual variation and growth parameters associated with each group (Muthén and Muthén, 2000). Specifically, the LGMM approach does not assume individuals coming from a homogenous population or equal variance within each group. Instead, it explicitly identifies heterogeneous growth curves and allows within-person variability, permitting flexibility and precision in mapping various forms of response trajectories over time. The LGMM approach has been increasingly adopted by studies examining pathways of psychological adjustment following health hazards, including spinal cord injury (Bonanno et al., 2012a), emergency surgery for traumatic injury (DeRoon-Cassini et al., 2010), disease epidemic (Bonanno et al., 2008), and cancer diagnosis and treatment (Helgeson et al., 2004; Lam, et al., 2010; Hou et al., 2010).

The best-fitting model was selected based on an integrative consideration of fit indices, theoretical predictions and generalizability (Muthén, 2004). We examined the Akaike (AIC), Bayesian (BIC), and sample size-adjusted Bayesian Information Criterion (SSBIC) indices, the entropy value, the *p* values of the Lo-Mendell-Rubin's adjusted likelihood ratio test (LRT) and the bootstrap likelihood ratio test (BLRT). Smaller AIC, BIC and SSBIC suggest better model fit; high entropy indicates reliability of latent groups; and significant LRT and BLRT of an estimated model suggest improvement in model fit compared to the one less class model. The conditional model with covariates (i.e., predictors) was selected based on the best-fitting unconditional model.

3. Results

3.1. Unconditional model

Table 2 summarized the fit indices of the one- to five-class models. The values of the three information criteria, AIC, BIC, and SSBIC decreased with increase of group number from one- to five-class solutions, suggesting improved fit. The entropy values were comparable for the five models. The *p* value of the LRT suggested improved model fit with each additional group. The BLRT, the most robust indicator of model-fit with large sample size (Nylund et al., 2007) indicated that the five-class solution was not significantly better fitting than the four-class solution. Examination of the patterns of the trajectories revealed that the additional group captured by the five-class solution was conceptually similar to the other group in the model with a slightly lower intercept at

Table 2

Fit indices for unconditional one- to five-class growth mixture models for depression.

Fit indices	AIC	BIC	SSA-BIC	LRT <i>p</i> value	BLRT <i>p</i> value	Entropy
1 Class	33,971.32	34,039.53	34,001.40	< 0.001	< 0.001	–
2 Classes	32,979.35	33,070.29	33,019.46	< 0.001	< 0.001	0.936
3 Classes	32,606.75	32,720.42	32,501.38	< 0.001	< 0.001	0.893
4 Classes	32,376.34	32,501.37	32,431.48	< 0.001	< 0.001	0.893
5 Classes	32,184.55	32,332.32	32,249.71	< 0.001	0.240	0.882

Note. AIC = Akaike Information Criterion; BIC = Bayesian Information Criterion; SSA-BIC = Sample Size Adjusted Bayesian Information Criterion; LRT = Lo-Mendell-Rubin Likelihood Ratio Test; and BLRT = Bootstrap Likelihood Ratio Test.

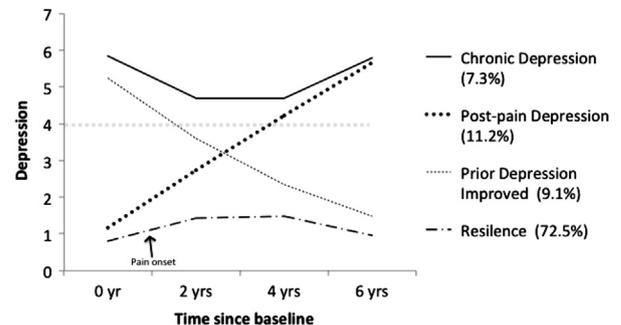


Fig. 1. Trajectories of depression symptoms pre- and post-pain onset over a six-year period (Unconditional Model). The light gray dotted line represents clinical cutoff.

the baseline. Consistent with recommendations for mixture model testing (Muthén, 2004), we chose to adopt the four-class model for parsimony and theoretical interpretability.

As shown in Fig. 1, the four-class solution identified four distinct trajectories of depressive symptoms prior to and following pain onset over the course of six years. The most common group was characterized by a *resilience* trajectory (72.5%), with minimal depression symptoms over the course of approximately one year prior to and five years post pain onset. The second group described a *post-pain depression* trajectory (11.2%) of low depression at baseline and increasing symptoms following pain onset. The third group, *chronic depression* (7.3%), described a trajectory of consistently high depression symptoms pre- and post-pain onset. A trajectory of *prior depression improved* trend (9.1%) emerged in the analysis, with high depression at the baseline but gradually declining symptoms following pain onset.

3.2. Conditional model

Covariates of interest were then entered into the four-class model for their possible inclusion in the conditional model. Pain-related functional impairment, perceived health and chronic illness prior to (BL) and following pain onset (T1), were all significantly related to the depression trajectories. Among the demographic variables, only gender and age were significant and retained in the model. The proportions and forms of the four depression trajectories (*resilience*, 72.0%; *prior depression improved*, 9.8%; *post-pain depression*, 11.4%; *chronic depression*, 6.8%; Fig. 2) were comparable to those captured by the unconditional model.

3.3. Predictors of group membership

The odd ratios and 95% confidence intervals of group comparisons are summarized in Table 3. Compared to the *resilience* group, the *post-pain depression* group was more likely to be female

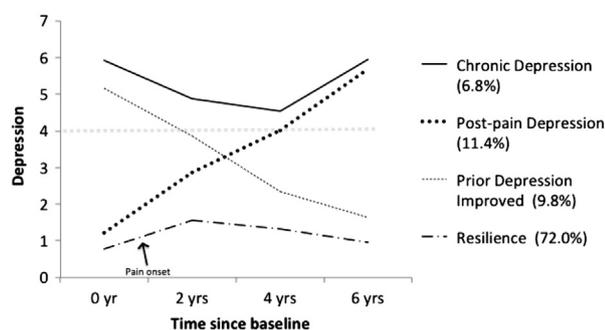


Fig. 2. Trajectories of depression symptoms pre- and post-pain onset over a six-year period (Conditional Model). The light gray dotted line represents clinical cutoff.

(OR=1.46, $p < 0.05$), and had worse perceived health both prior to (BL; OR=0.82, $p < 0.05$) and following pain onset (T1; OR=0.75, $p < 0.01$). There was no difference in functional impairment and number of chronic illnesses between the two groups. The *prior depression improved* group reported worse health both at BL (OR=0.68; $p < 0.01$) and at T1 (OR=0.68; $p < 0.01$), and they also reported *more* chronic illnesses at BL (OR=1.35, $p < 0.01$) and *fewer* illnesses at T1 (OR=0.71, $p < 0.01$), compared to the *resilience* group. The *chronic depression* group was more likely to be female (OR=2.14, $p < 0.01$), younger (OR=0.94, $p < 0.05$), and to report functional impairment (OR=1.69, $p < 0.05$) and worse health at BL (OR=0.42; $p < 0.001$), compared to the *resilience* group. Compared to the *post-pain depression* group, the *prior depression improved* group was older (OR=1.06, $p < 0.05$), and had *more* illnesses at BL (OR=1.38; $p < 0.05$) and *fewer* illnesses at T1 (OR=0.64; $p < 0.01$). The only difference observed between the *chronic depression* and *post-pain depression* groups was that the former group perceived worse health at BL (OR=0.52; $p < 0.001$). Finally, individuals with *chronic depression* were younger (OR=0.92, $p < 0.01$) and perceived worse health at BL (OR=0.62; $p < 0.05$) than those who showed improvement in depression after pain onset (i.e., *prior depression improved*).

3.4. Secondary analysis

Our primary goal of the study was to examine depression responses to pain onset, thus pain occurrences at later follow-ups (i.e., T2 and T3) were not included in the model. Given the consideration that there might exist a reciprocal relationship between pain and depression (e.g., Bair et al., 2003; Fishbain et al., 1997), we conducted a secondary analysis including pain occurrences at T3 as an additional covariate in the conditional model to examine the impact of depression on pain. The model showed improved fit compared to the conditional model ($\chi^2=622.426$, $p < 0.001$), but the proportions of the four classes were similar to those in the conditional model (*resilience*, 69.1%; *post-pain depression*, 14.1%; *prior depression improved*, 11.4%; *chronic depression*, 5.3%). The majority of the sample still reported pain at the sixth-year follow-up (50% for the *resilience* group, 60% for the *prior depression improved* group, 70% for *post-pain depression* group and 80% for the *chronic depression* group, respectively).

4. Discussion

Using a growth mixture modeling approach, we identified four distinct depression trajectories over the course of a six-year period beginning approximately one year prior to and five years following the onset of moderate-to-severe pain in a large nationally representative sample. The unconditional and conditional models

yielded comparable results in terms of the form and prevalence of each trajectory, attesting to the validity and stability of the four patterns of adjustment. The most common outcome, accounting for more than two-thirds of the sample, was characterized by a stable trajectory with virtually no or minimal depression symptoms before and after pain occurrence (i.e., *resilience*). The high prevalence of complete absence of depression among individuals who experienced frequent pain of higher intensities calls for more research attention to this form of adjustment to better understand the mechanisms as well as moderators between pain experience and psychological responses (Karoly and Ruehlman, 2006; Strugeon and Zautra, 2010; Yeung et al., 2012).

Two distinct pathways emerged among people who exhibited depression symptom elevation. About 11% of the sample exhibited a trajectory that shifted from no depression symptoms prior to pain to increasingly clinically relevant symptoms following pain onset (i.e., *post-pain depression*), and a small proportion of the sample exhibited consistently high level of depression, with minor fluctuation during the course, both prior to and following pain onset (i.e., *chronic depression*).

A trajectory of improved depression following pain onset emerged unexpectedly and accounted for a significant proportion of the sample (i.e., *prior depression improved*; 9.8%). The interpretation of this response pattern was less straightforward. Individuals in this group were older than those who had chronic depression and those who showed depression symptom elevation following pain. Older adults are less likely to acknowledge or seek help for depression (Murrell et al., 1983), thus they may have to rely on their own capacity to cope with the mental disorder. On the other hand, physical symptoms, such as pain, are widely recognized as increasing with age. The onset of pain therefore may, inadvertently, serve as a legitimate cause for role adjustment and support seeking for older adults, leading to recovery of depression through the mechanism of secondary gain from somatic expression (Fishbain et al., 1995).

Another possible explanation came from the finding that this group had *more* pre-pain and *fewer* post-pain chronic illnesses, compared to the *post-pain depression* group and the *resilience* group. It was possible that pain reported by this group was caused by medical procedures (e.g., surgery) that were part of the treatment for prior illnesses, and the healing of these illnesses might explain the reduction in depressive symptoms. The pattern of distress followed by improvement has been identified by multiple studies investigating psychological adjustment to challenging events with prospective data, including conjugal bereavement (Bonanno et al., 2002; Galatzer-Levy and Bonanno, 2012), and military and police deployments (Bonanno et al., 2012a, 2012b; Dickstein et al., 2010; Galatzer-Levy et al., 2013). More convincing explanation of the *prior depression improved* trajectory requires comprehensive inspection of various pre- and post-pain predictors.

Except for its value in predicting the *prior depression improved* group, chronic illness was not associated with other trajectory patterns. Functional impairment, a factor generally regarded as an important predictor of pain and depression comorbidity (Bair et al., 2003, 2008; Gureje et al., 2001; Hilderink et al., 2012; Poleshuck et al., 2009) was found to only separate the chronically depressed and resilience groups. One possible cause for the discrepancy might be in the different assessment methods used in the current study and previous studies. The impact of functional impairment may operate on a more graded level for depression development. The use of a binary measure in the current study might have failed to adequately capture more nuanced effects.

Self-perceived health emerged as the strongest predictor for individuals in the *resilience* group: they reported better health

Table 3
Multinomial logistic regression predicting class membership.

	Resilience vs.					
	Post-pain depression		Prior depression improved		Chronic depression	
	OR	95% CI	OR	95% CI	OR	95% CI
Gender	1.46	(1.01, 2.11)	1.23	(0.84, 1.80)	2.14	(1.28, 3.58)
Age at pain onset	0.97	(0.93, 1.00)	1.03	(0.98, 1.07)	0.94	(0.90, 0.99)
Function impairment at T1	1.19	(0.83, 1.73)	1.32	(0.90, 1.92)	1.69	(1.01, 2.82)
Perceived health at BL	0.82	(0.68, 0.98)	0.68	(0.54, 0.87)	0.42	(0.31, 0.57)
Perceived health at T1	0.75	(0.61, 0.92)	0.68	(0.54, 0.86)	0.88	(0.65, 1.19)
Chronic illness at BL	0.98	(0.82, 1.17)	1.35	(1.08, 1.68)	1.08	(0.86, 1.34)
Chronic illness at T1	1.11	(0.93, 1.34)	0.71	(0.57, 0.90)	0.92	(0.74, 1.13)
	Post-pain depression vs.		Chronic depression improved vs.		Chronic depression	
	Prior depression improved		Chronic depression		Chronic depression	
	OR	95% CI	OR	95% CI	OR	95% CI
Gender	0.84	(0.52, 1.37)	1.47	(0.79, 2.71)	1.73	(0.90, 3.35)
Age at pain onset	1.06	(1.01, 1.12)	0.97	(0.92, 1.03)	0.92	(0.86, 0.98)
Function impairment at T1	1.10	(0.67, 1.80)	1.41	(0.76, 2.62)	1.28	(0.66, 2.50)
Perceived health at BL	0.84	(0.64, 1.10)	0.52	(0.36, 0.73)	0.62	(0.42, 0.90)
Perceived health at T1	0.91	(0.67, 1.23)	1.17	(0.83, 1.67)	1.29	(0.85, 1.96)
Chronic illness at BL	1.38	(1.06, 1.80)	1.11	(0.85, 1.43)	0.80	(0.58, 1.10)
Chronic illness at T1	0.64	(0.49, 0.84)	0.82	(0.64, 1.06)	1.28	(0.95, 1.74)

both pre- and post-pain compared to those who developed depression following pain and those whose prior depression improved following pain, and better pre-pain health compared to the *chronic depression* group. Our results were comparable with previous studies using population-based pain samples where self-rated health was found to predict depression cross-sectionally (Molarius and Janson, 2002) and in the short-term (Carroll et al., 2003). Self-perceived health has been shown to be correlated with a myriad of psychosocial factors beyond its association with medical conditions, including chronic stress, and sense of mastery and control (Cott et al., 1999). The current finding that subjective perception of good health despite pain and other illnesses significantly reduced the likelihood of depression underscores the role of psychological and social resources in the long-term adjustment to pain (Gatchel, 2004).

Another intriguing result related to self-rated health was that the *chronic depression* group tended to perceive worse health at baseline but similar health status following pain onset, when compared to the other three groups; whereas the *post-pain depression* group perceived worse health both before and after pain, compared to the *resilience* group. It is noted that these two findings were independent of actual physical illnesses, suggesting that people who suffer from longer-term depression may have more generic health-related concerns whereas those who showed depression symptomatology following pain onset may be troubled by both generic and pain-specific health concerns. This insight provides useful information in implementing clinical interventions with the two distinct groups that exhibited concurrent pain and depression.

Results of the demographic variables were less clear-cut. Income, ethnicity, marriage and employment status did not separate the groups. The *post-pain depression* and *chronic depression* groups were more likely to be females, compared to the *resilience* group, and to be younger, compared to the *prior depression improved* group. These findings were compatible with previous studies that identified female gender and younger age as risk factors for depression among pain patients (Miller and Cano, 2009; Patten, 2001).

Our primary goal was to investigate depression response to pain onset, thus pain occurrences at the two follow-ups were not

included in the final model. We did however conduct a secondary analysis including distal pain occurrence six years since baseline as a covariate in the model. The models with and without distal pain rendered compatible results, suggesting the stability of the four trajectories. It should be noted that our results do not preclude a mutually maintaining relationship between pain and depression. The finding that individuals who exhibited elevated depression symptoms following pain onset (i.e., *chronic depression* and *post-pain depression*) had higher rates of enduring pain than those with no or improved depression suggests that presence of depression may indeed prolong pain experiences. Future studies may employ the mixture modeling technique to examine the patterns of pain development among individual with depression to gain more insights into the possible dynamic relationship between the two conditions (Bair et al., 2003; Fishbain et al., 1997).

Research on psychological adjustment to pain typically defines pain as a health condition when it persists more than one or three months (Tunks et al., 2008; Pengel et al., 2003). We included in the study individuals who reported frequent pain within a two-year period from baseline. It was believed that the majority of the sample had pain durations longer than one month as the frequencies of pain duration were likely to be evenly distributed over the two-year period. In addition, we heightened the clinical relevance of the sample by including only individuals with moderate or severe pain intensity (Jensen et al., 1986). However, the possible inclusion of a small proportion of individuals experiencing transient pain might have slightly inflated the resilient trajectory.

Another limitation of the study was the uncertainty around the cause, type and sites of pain. While various pain conditions are generally considered to be a global clinical phenomenon rather than discrete entities (Addison, 1984; Macfarlane, 1999), supporting the validity of mapping depression responses in a broad pain population, several studies have shown that multiple pain sites as well as specific types of pain could increase the risk for depression (Bair et al., 2003; Gureje et al., 2001). Thus, it is important to bear in mind the specific characteristics of pain and their associated risks when applying the current results in assessing depression outcomes among pain patients. In addition, the lack of information on medications or

treatments the individuals might be taking for pain or depression might also, to some extent, have impacted the trajectories.

Notwithstanding these limitations, this is the first study to systematically investigate heterogeneous long-term depression responses to chronic pain using prospective data. The identification of stable low depression as the modal response calls for more research on resilient, or healthy adjustment to the potentially debilitating experience of pain (Karoly and Ruhlman, 2006; Strugeon and Zautra, 2010; Yeung et al., 2012). The demarcation of individuals who showed chronic depression and those who developed depression following pain, as well as distinct factors associated with each pathway, renders important information for early screening and intervention for depression development in pain patients. Finally, the finding that perceived health, but not chronic illness or functional impairment, predicted healthy adjustment to pain, highlights the impact of psychosocial factors in mediating pain and depression.

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