Clinical pain research

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# The impact of comorbid pain and depression in the United States: results from a nationally representative survey

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**Abstract**

**Background and aims:** The co-morbidity between pain and depression is a target of interest for treatment. However most of the published literature on the topic has used clinical cohorts as the population of interest. The goal of this study was to use a nationally representative sample to explore how health outcomes varied across pain and depression status in a cohort sampled from the general US population.
**Methods:** This was a cross-sectional analysis of adults ≥18 years in the 2009–2010 National Health and Nutrition Examination Survey. The cohort was stratified into: no pain/depression, pain alone, depression alone, and pain with depression. The primary outcome was self-reported general health status, and secondary outcomes were healthcare visits, overnight hospital stays and functional limitation. Survey weighted logistic regression was used to adjust for potential confounders.
**Results:** The cohort consisted of 4,213 individuals, of which 186 (4.4%) reported concurrent pain and depression. 597 (14.2%) and 253 (6.0%) were classified with either pain or depression alone, respectively. The majority of individuals with co-morbid pain and depression reported poor health (65.1%, $p < 0.001$) and were significantly more likely than those with neither condition to rate their health as poor after adjustment (OR: 7.77, 95% CI: 4.24–14.26, $p < 0.001$). Those with pain only or depression only were also more likely to rate their health as poor, albeit to a lesser extent (OR: 2.21, 95% CI: 1.21–2.34, $p < 0.001$; OR: 3.75, 95% CI: 2.54–5.54, $p < 0.001$, respectively). A similar pattern was noted across all secondary outcomes. Most notably, those with co-morbid pain and depression were the most likely to endorse functional limitation (OR: 13.15, 95% CI: 8.00–21.61, $p < 0.001$). Comparatively, a similar trend was noted amongst those with pain only or depression only, though with a reduced effect size (OR: 4.23, 95% CI: 3.12–4.77, $p < 0.001$; OR: 5.13, 95% CI: 3.38–7.82, $p < 0.001$).
**Conclusions:** Co-morbid pain and depression in the general population resulted in markedly worse outcomes versus isolated pain or depression. Further, the effect appears to be synergistic. Given the substantial burdens of pain and depression, future treatments should aim to address both conditions simultaneously.
**Implications:** As a result of the co-morbidity between pain and depression, patients presenting with either condition should increase the index of suspicion among clinicians and prompt screening for the reciprocal condition. Early intervention for co-morbid pain and depression has the potential to mitigate future incidence of chronic pain and major depression.

**Keywords:** depression; chronic pain; health status; healthcare utilization.

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# 1 Introduction

Individually, pain and depression are conditions that contribute significantly to the global burden of disease [1, 2]. The lifetime prevalence of depression varies considerably from country to country but is estimated to be between 6.5% and 21.0%, while the lifetime prevalence of chronic pain symptoms ranges from 24% to 37% [2, 3]. In both cases, the personal, social and economic burdens of these conditions are significant with depression alone accounting for nearly 25% of the global burden of disease and several hundreds of billions of dollars annually [4, 5].

Importantly, pain and depression are often co-morbid, as there is a significant proportion of individuals with depression who report pain and *vice versa*. For example, over 65% of individuals suffering from depression report symptoms of pain while over 60% of individuals with pain endorse symptoms of depression [6, 7]. This reciprocal relationship between chronic pain and depression results in a prognosis that is worse than either condition alone as pain can negatively impact the course and treatment of depression and depression can do the same for pain [8, 9]. This impact manifests itself as a lower quality of life and increased healthcare usage/costs [5, 10].

The relationship between pain and depression was recognized long ago [11] and has recently started to become a focus of treatment. However, much of the work regarding co-morbid pain and depression has been conducted on cohorts of patients already diagnosed with either pain or depression and then subsequently assessed for the reciprocal condition [6, 12–14]. This study aims to characterize self-reported health status and healthcare utilization for comorbid pain and depression within a nationally representative sample using the 2009–2010 National Health and Nutrition Examination Survey (NHANES) cohort.

# 2 Methods

## 2.1 Study population

Data for the study were obtained from NHANES. NHANES data were selected as they are robust, publicly available datasets with a diverse set of clinical measurements and risk factors that are shared across a wide variety of populations. Since 1999, the NHANES surveys have been administered annually in the US by the National Center for Health Statistics (NCHS) in conjunction with the Centers for Disease Control and Prevention (CDC). These surveys are used to assess health and nutrition status in the US population corresponding to the most recent census data and the databases themselves are available publicly through the CDC's website. The program was approved by the NCHS Ethics Review Board and all participants provided informed consent prior to being interviewed. A dataset for this study was constructed using files from the 2009 to 2010 NHANES. The population consisted of all respondents age 18 years or older and any respondents with missing data were excluded from the analysis.

## 2.2 Exposure

Self-reported depression and chronic pain were the co-primary exposures for this study. Both variables were treated as binary and used to stratify the patient population into the following groups: neither pain nor depression, pain only, depression only, and comorbid pain and depression. Chronic pain was defined as an individual self-reporting current pain in any area of the body that has persisted for at least 3 months (i.e. "Was there one time when you had pain, aching or stiffness in your neck on almost every day for 3 months in a row?") [15]. The Patient Health Questionnaire-9 (PHQ-9) is administered by NHANES surveyors to determine a classification of depression, with a score of ≥10 on the PHQ-9 being considered indicative of clinically meaningful depression [16]. The PHQ-9 is a well validated measure that addresses the nine symptoms of a major depressive episode and is commonly used to define depression in clinical studies [17].

## 2.3 Outcomes

The primary outcome for this study was self-rated health. Although there are numerous biological, physiological, psychological, behavioral and health underpinnings of self-rated health, the primary outcome of self-rated health is considered a valid measure across various populations [18]. In the NHANES study, participants are asked to rate their health as "excellent, very good, good, fair or poor." For this study, these responses were dichotomized to good (excellent, very good or good) and poor (fair or poor).

Secondary outcomes for this study included: self-reported number of healthcare visits in the past 12 months (defined as: "≤3" or ">3"), self-reported overnight hospital stay in the past 12 months (defined as: "yes" or "no")

and any self-reported functional limitation resulting from the pain (defined as: "yes" or "no"). These outcomes were chosen for this analysis as they capture the physical, social and economic impact of co-morbid pain and depression.

### 2.4 Covariates

Covariates were selected a priori based on biologic plausibility of being a confounder in the relationship between exposure and outcome. The selected covariates included age (in years, at screening), sex, marital status (defined as married/living with partner, separated/divorced/widowed, never married), race (Hispanic, non-Hispanic white, non-Hispanic black, other), ratio of family income to poverty level (continuous variable), and BMI coded into categories (<25 kg/m$^2$, 25–30 kg/m$^2$, and >30 kg/m$^2$).

### 2.5 Data analysis

Unadjusted analysis of differences in baseline covariates and outcomes across exposure groups was undertaken using chi-square and ANOVA tests, where appropriate. Multivariable logistic regression was employed to determine the association between the exposure and outcome while adjusting for potential confounders. Regression models were performed with the incorporation of survey weights. All covariates were included in the model without further selection. For continuous variables (age and ratio of family income to poverty level), a quadratic term was also included to adjust for potential non-linear associations. Data from the regression analyses were used to create a predicted probability model to illustrate the relationship between exposures and outcomes.

A significant portion ($n = 664$) of missing data was due to blank responses on the PHQ-9. To determine the impact of this missing data, a *post-hoc* sensitivity analysis was conducted. Missing data were recoded via two methods: 1) missing values were assigned a maximum value of 3 for the relevant question and 2) missing values were assigned a minimum value of 0 for the relevant question. The sensitivity analysis was then conducted on both sets of recoded data.

Significance was tested through two-tailed tests at a level of $p < 0.05$ significance. All data analyses were performed using Stata Version 15.1 (StataCorp, College Station, TX, USA).

## 3 Results

The cohort consisted of 5,001 individuals; 788 (15.8%) were excluded due to missing data leaving a total of 4,213 respondents, of whom 3,177 (75.4%) met threshold criteria for neither depression nor pain, 597 (14.2%) were classified with chronic pain only and 253 (6.0%) were classified with depression only. The remaining 186 (4.4%) participants met criteria for co-morbid pain and depression. Significant differences across exposure categories emerged amongst several covariates. Obesity was most prevalent amongst the co-morbid group as 53.8% of individuals had a body mass index (BMI) in excess of 30 kg/m$^2$. The mean ratio of family income to poverty level was similar between the neither and pain only categories ($2.6 \pm 1.7$ and $2.4 \pm 1.7$, respectively) and was also similar between the depression only and co-morbid groups ($1.7 \pm 1.5$ and $1.7 \pm 1.4$, respectively). Smoking was most prevalent amongst the co-morbid group with 45.7% of individuals reporting cigarette use. A complete list of these differences is presented in Table 1. Individuals in the co-morbid group were the most likely to rate their health as poor, with 65.1% of individuals doing so. In comparison, 46.6% of those with depression rated their health as poor and 32.2% of those with pain did the same. Of those in the neither category, 17.1% rated their health as poor. A full summary of outcomes by exposure category is presented in Table 2.

After adjusted logistic regression, compared to individuals with neither condition, individuals with co-morbid pain and depression had 7.77 greater odds of reporting poor health (95% CI: 4.24–14.26, $p < 0.001$). Those with pain alone had double the odds of reporting poor health (OR: 2.21, 95% CI: 1.63–3.02, $p < 0.001$) while the effect size for patients with depression alone was quadruple the odds (OR: 3.75, 95% CI: 2.54–5.54, $p < 0.001$). With respect to functional limitation, individuals with pain and depression had 13.15 greater odds of reporting limits on daily activity (95% CI: 8.00–21.61, $p < 0.001$) while those with pain or depression alone had quadruple (OR: 4.24, 95% CI: 3.12–5.77, $p < 0.001$) and quintuple (OR: 5.13, 95% CI: 3.38–7.82, $p < 0.001$) the odds, respectively. Similar results were found across all other secondary outcomes. A full summary of the regression analysis is presented in Table 3. When transforming odds ratios into predicted probabilities, there was a synergistic relationship between depression and chronic pain. The results of this transformation are provided in Fig. 1. When patients with missing PHQ-9 values were re-coded in the *post-hoc* sensitivity analysis, no material changes in effect size and statistical significance were noted compared to the primary analysis.

**Table 1:** Descriptive statistics of adults aged ≥18 years in NHANES 2009–2010.

| | | Neither | Pain | Depression | Pain ± depression | *p*-Value |
|---|---|---|---|---|---|---|
| *n* | 4,213 | 3,177 (75.4%) | 597 (14.2%) | 253 (6.0%) | 186 (4.4%) | |
| Age (years) at screening – mean (±SD) | | 43.5 (±14.3) | 47.2 (±13.6) | 42.5 (±14.0) | 47.2 (±12.1) | <0.001 |
| Gender | Female | 1,511 (47.6%) | 314 (52.6%) | 165 (65.2%) | 117 (62.9%) | <0.001 |
| Race | Hispanic | 968 (30.5%) | 148 (24.8%) | 91 (36.0%) | 53 (28.5%) | <0.001 |
| | Non-Hispanic white | 1,413 (44.5%) | 343 (57.5%) | 99 (39.1%) | 87 (46.8%) | |
| | Non-Hispanic black | 610 (19.2%) | 88 (14.7%) | 48 (19.0%) | 37 (19.9%) | |
| | Other | 186 (5.9%) | 18 (3.0%) | 15 (5.9%) | 9 (4.8%) | |
| Body mass index | <25 | 999 (31.4%) | 157 (26.3%) | 86 (34.0%) | 39 (21.0%) | <0.001 |
| | 25–30 | 1,124 (35.4%) | 211 (35.3%) | 61 (24.1%) | 47 (25.3%) | |
| | >30 | 1,054 (33.2%) | 229 (38.4%) | 106 (41.9%) | 100 (53.8%) | |
| Marital status | Married/living with partner | 1,995 (62.8%) | 375 (62.8%) | 118 (46.6%) | 91 (48.9%) | <0.001 |
| | Divorced/ separated/widowed | 524 (16.5%) | 125 (20.9%) | 69 (27.3%) | 64 (34.4%) | |
| | Never married | 658 (20.7%) | 97 (16.2%) | 66 (26.1%) | 31 (16.7%) | |
| Insurance | Private | 1,552 (48.9%) | 232 (38.9%) | 69 (27.3%) | 42 (22.6%) | <0.001 |
| | Medicare | 178 (5.6%) | 59 (9.9%) | 17 (6.7%) | 28 (15.1%) | |
| | Medicaid | 174 (5.5%) | 70 (11.7%) | 36 (14.2%) | 42 (22.6%) | |
| | Other | 354 (11.1%) | 85 (14.2%) | 30 (11.9%) | 25 (13.4%) | |
| | None | 919 (28.9%) | 151 (25.3%) | 101 (39.9%) | 49 (26.3%) | |
| Ratio of family income:poverty level – mean (±SD) | | 2.6 (±1.7) | 2.4 (±1.7) | 1.7 (±1.5) | 1.7 (±1.4) | <0.001 |
| Alcohol use | Yes | 1,654 (52.1%) | 305 (51.1%) | 156 (61.7%) | 114 (61.3%) | 0.002 |
| Cigarette use | Yes | 681 (21.4%) | 176 (29.5%) | 101 (39.9%) | 85 (45.7%) | <0.001 |
| Diabetes | Yes | 312 (9.8%) | 88 (14.7%) | 42 (16.6%) | 41 (22.0%) | <0.001 |
| Stroke | Yes | 62 (2.0%) | 16 (2.7%) | 8 (3.2%) | 13 (7.0%) | <0.001 |
| Coronary artery disease | Yes | 60 (1.9%) | 24 (4.0%) | 8 (3.2%) | 6 (3.2%) | 0.009 |
| Cancer | Yes | 178 (5.6%) | 57 (9.5%) | 14 (5.5%) | 22 (11.8%) | <0.001 |

$\chi^2$-analysis used for categorical variables.
ANOVA used for continuous variables.

**Table 2:** Outcome categories by pain-depression status for adults aged ≥18 years in NHANES 2009–2010.

| | | Neither | Pain | Depression | Pain ± depression | *p*-Value |
|---|---|---|---|---|---|---|
| *n* | 4,213 | 3,177 (75.4%) | 597 (14.2%) | 253 (6.0%) | 186 (4.4%) | |
| General health | Poor | 543 (17.1%) | 192 (32.2%) | 118 (46.6%) | 121 (65.1%) | <0.001 |
| # Healthcare visits (in past 12 months) | >3 | 952 (30.0%) | 281 (47.1%) | 119 (47.0%) | 115 (61.8%) | <0.001 |
| Overnight stay in hospital (in past 12 months) | Yes | 282 (8.9%) | 88 (14.7%) | 56 (22.1%) | 55 (29.6%) | <0.001 |
| Functional limitation | Yes | 316 (9.9%) | 211 (35.3%) | 95 (37.5%) | 118 (63.4%) | <0.001 |

$\chi^2$-analysis used for categorical variables.
ANOVA used for continuous variables.

Supplementary Tables S1–S6 describe the results of the *post-hoc* sensitivity analysis.

## 4 Discussion and conclusion

The results of this study demonstrate that those with concurrent pain and depression were the most likely subgroup to report their health as poor. While those with pain or depression also exhibited a significant association with sub-optimal health, the effect was significantly greater for the co-morbid subgroup. The same trend was noted across all secondary outcomes as well, with the co-morbid pain and depression subgroup reporting increased healthcare utilization, more frequent overnight hospitalization and increased limitation on daily functioning. Furthermore,

**Table 3:** Weighted and adjusted odds ratios for associations between pain-depression status and outcome category.

| Exposure group | General health | | # of Healthcare visits (in past 12 months) | | Overnight hospital stay (in past 12 months) | | Functional limitation | |
|---|---|---|---|---|---|---|---|---|
| | OR (95% CI) | *p*-Value | OR (95% CI) | *p*-Value | OR (95% CI) | *p*-Value | OR (95% CI) | *p*-Value |
| Neither | 1 (ref) | | 1 (ref) | | 1 (ref) | | 1 (ref) | |
| Pain | 2.21 (1.63–3.02) | <0.001 | 1.68 (1.21–2.34) | 0.004 | 1.32 (0.87–2.01) | 0.175 | 4.24 (3.12–5.77) | <0.001 |
| Depression | 3.75 (2.54–5.54) | <0.001 | 2.48 (1.84–3.36) | <0.001 | 2.11 (1.25–3.58) | 0.008 | 5.13 (3.38–7.82) | <0.001 |
| Pain ± depression | 7.77 (4.24–14.26) | <0.001 | 3.24 (2.01–5.25) | <0.001 | 2.59 (1.21–5.55) | 0.017 | 13.15 (8.00–21.61) | <0.001 |

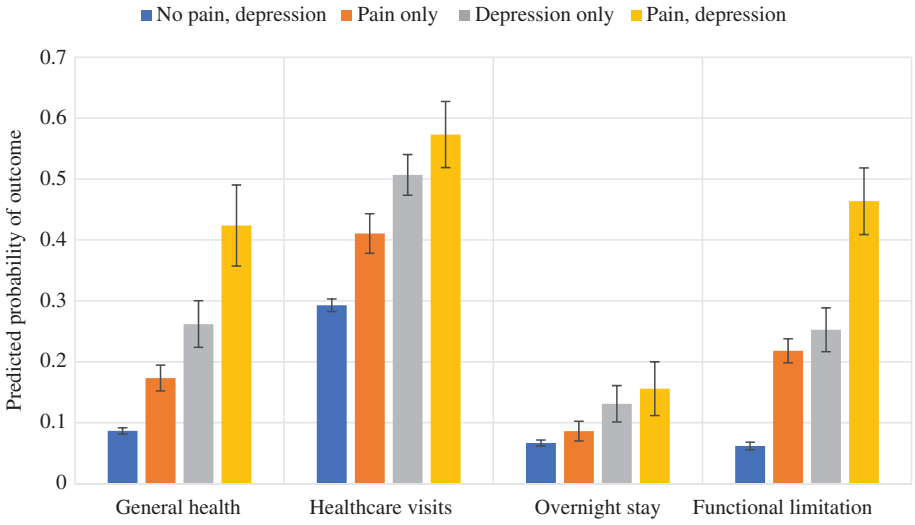


**Fig. 1:** Predicted probabilities calculated from survey weighted adjusted logistic regression models holding all other covariates at their mean value. Regression models were constructed using covariates presented in Table 1. Quadratic terms were added to continuous variables to adjust for non-linear associations. Outcomes were defined as follows: (1) General Health – Good vs. Poor, (2) # of Healthcare Visits in the Past 12 Months – ≤3 vs. >3, (3) Any Overnight Stay in Hospital in the Past 12 Months – Yes vs. No, (4) Any Functional Limitation Resulting from Pain and/or Depression – Yes vs. No.

the relationship between pain and depression appears to be synergistic as the effect size of the comorbid condition is greater than the sum of the two conditions in isolation [19]. For example, individuals with pain alone were four times as likely to endorse functional limitation while those with depression alone were five times as likely to do the same. In contrast, those with both conditions together were more than 13 times as likely to endorse functional limitation, suggesting that there is some interaction between the two conditions.

Our results support previous findings that health-related outcomes are worse amongst individuals with pain and depression in comparison to those with either condition in isolation [6, 13, 14, 20]. Additionally, we confirm that concurrent pain and depression status is predictive of increased healthcare utilization, as has been previously suggested in the literature [10, 21]. The lower prevalence of pain and depression in our cohort, compared with previous work [22, 23] likely stems from our use of a general population rather than a clinical cohort consisting of individuals presenting with pain and being evaluated for depression or *vice versa*. Indeed, our study is one of a small number to have examined the effect of comorbid pain and depression within the general population [14, 15, 24]. To our knowledge, we are the first group to quantify the relationship of comorbid pain and depression to self-rated health and functional limitation using a cohort sampled from the general population.

Several notable relationships between covariates and pain/depression status existed amongst our results that suggest avenues for further research. For instance, the prevalence of obesity was highest amongst the comorbid group as nearly half of the group were classified with a BMI in excess of 30 kg/m$^2$. Other studies have concluded that both pain and depression have some correlation with obesity [25, 26] and it would appear that the interaction

between pain and depression is also correlated with obesity. Additionally, the ratio of family income to poverty index was lowest amongst individuals with comorbid pain and depression as well as those with depression alone. Being a social determinant of health, this finding suggests that those with co-morbid pain and depression or simply depression alone, may be more likely to economically and/or socially disadvantaged and be less able to access treatment as a result. Finally, cigarette use was highest amongst the co-morbid group. Nicotine use is well associated with pain and tends to increase with increasing pain; our work supports the notion that co-morbid pain and depression is also indicative of increasing nicotine use [27, 28].

Owing to the co-morbidity between pain and depression, patients presenting with either of the two conditions should increase the index of suspicion among clinicians to screen for the reciprocal condition. This is particularly important in light of the healthcare utilization and cost-effectiveness data presented here and elsewhere in the literature [10, 21]. Interventions for concurrent pain and depression have significant implications for health status and resource utilization/allocation [20, 29] and as such it is important to promote further research into simultaneous therapeutics that target both depression and pain as first-line interventions. Indeed, a previous review on this subject concluded that early interventions for co-morbid pain and depression can help prevent chronic pain and major depressive disorders [30].

The strengths of this study are its use of a large, nationally representative sample and rich covariate data. Additionally, the results were consistent across several different outcomes and the weighting and survey methodology employed in the NHANES ensures its generalizability to the general population. However, the study has several limitations inherent in its design that should be considered when interpreting the results. Firstly, outcomes were self-reported and there was no clinical exam or interview for pain nor for depression. Secondly, given that the study was cross-sectional, unmeasured confounding is a concern. At the same time, this would be unlikely to significantly change the results given the magnitude of the effect sizes discovered. We also did not have data on the intensity/severity, chronicity, type and etiology of the pain and thus those who reported pain on the questionnaire might have more severe disease thus overestimating our result (for example, more people in the pain and depression category have cancer). Additionally, we lacked information regarding prescription analgesic usage which may partially explain the high prevalence of obesity amongst the pain and depression subgroup. Finally, our data are relatively old; however, they are the most recent data in NHANES that had information on both pain and depression. Further, it is unlikely that the interaction between these two conditions would have changed significantly over time due to their neurophysiological overlap.

This study contrasts healthcare outcomes amongst a general population stratified for pain, depression, neither or both conditions. Our findings indicate that while pain and depression alone result in sub-optimal outcomes, the effect of both conditions is far greater than each alone. Our results firmly establish the reciprocal nature of pain and depression and their impact on health. Given the tremendous personal, social and economic burden that chronic pain and depression extoll on individuals and healthcare systems safe and effective therapeutics to simultaneously treat pain and depression are needed. Prospective studies should strive to validate the use of such interventions for this particular condition.

**Authors' statements**

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## References

[1] WHO. Depression: fact sheet. Available at: http://www.who.int/mediacentre/factsheets/fs369/en/. Accessed: 24 July 2018.

[2] Regier DA, Myers JK, Kramer M, Robins LN, Blazer DG, Hough RL, Eaton WW, Locke BZ. The NIMH Epidemiologic Catchment Area program. Historical context, major objectives, and study population characteristics. Arch Gen Psychiatry 1984;41:934–41.

[3] Kessler RC, Bromet EJ. The epidemiology of depression across cultures. Annu Rev Public Health 2013;34:119–38.

[4] GBD 2013 DALYs and HALE Collaborators. Global, regional, and national disability-adjusted life years (DALYs) for 306 diseases and injuries and healthy life expectancy (HALE) for 188 countries, 1990–2013: quantifying the epidemiological transition. Lancet 2015;386:2145–91.

[5] Rayner L, Hotopf M, Petkova H, Matcham F, Simpson A, McCracken LM. Depression in patients with chronic pain attending a specialised pain treatment centre: prevalence and impact on health care costs. Pain 2016;157:1472–9.

[6] Bair MJ, Robinson RL, Katon W, Kroenke K. Depression and pain comorbidity: a literature review. Arch Intern Med 2003;163:2433–45.

[7] Katon W, Egan K, Miller D. Chronic pain: lifetime psychiatric diagnoses and family history. Am J Psychiatry 1985;142:1156–60.

[8] Simon GE, VonKorff M, Piccinelli M, Fullerton C, Ormel J. An international study of the relation between somatic symptoms and depression. N Engl J Med 1999;341:1329–35.
[9] Klinkman MS. Competing demands in psychosocial care. A model for the identification and treatment of depressive disorders in primary care. Gen Hosp Psychiatry 1997;19:98–111.
[10] Emptage NP, Sturm R, Robinson RL. Depression and comorbid pain as predictors of disability, employment, insurance status, and health care costs. Psychiatr Serv 2005;56:468–74.
[11] VonKorff M, Simon GE. The relationship between pain and depression. Br J Psychiatry 1996;168(S30):101–8.
[12] Bair MJ, Wu J, Damush TM, Sutherland JM, Kroenke K. Association of depression and anxiety alone and in combination with chronic musculoskeletal pain in primary care patients. Psychosom Med 2008;70:890–7.
[13] Kroenke K, Wu J, Bair MJ, Krebs EE, Damush TM, Tu W. Reciprocal relationship between pain and depression: a 12-month longitudinal analysis in primary care. J Pain 2011;12:964–73.
[14] Ang DC, Bair MJ, Damush TM, Wu J, Tu W, Kroenke K. Predictors of pain outcomes in patients with chronic musculoskeletal pain co-morbid with depression: results from a randomized controlled trial. Pain Med 2010;11:482–91.
[15] Hardt J, Jacobsen C, Goldberg J, Nickel R, Buchwald D. Prevalence of chronic pain in a representative sample in the United States. Pain Med 2008;9:803–12.
[16] Kroenke K, Spitzer RL. The PHQ-9: a new depression diagnostic and severity measure. Psychiatr Ann 2002;32:509–15.
[17] Kroenke K, Spitzer RL, Williams JB. The PHQ-9: validity of a brief depression severity measure. J Gen Intern Med 2001;16:606–13.
[18] Jylha M. What is self-rated health and why does it predict mortality? Towards a unified conceptual model. Soc Sci Med 2009;69:307–16.
[19] Robinson MJ, Edwards SE, Iyengar S, Bymaster F, Clark M, Katon W. Depression and pain. Front Biosci (Landmark Ed) 2009;14:5031–51.
[20] Outcalt SD, Kroenke K, Krebs EE, Chumbler NR, Wu J, Yu Z, Bair MJ. Chronic pain and comorbid mental health conditions: independent associations of posttraumatic stress disorder and depression with pain, disability, and quality of life. J Behav Med 2015;38:535–43.
[21] Pan YJ, Pan CH, Chan HY, Kuo KH. Depression and pain: an appraisal of cost effectiveness and cost utility of antidepressants. J Psychiatr Res 2015;63:123–31.
[22] Lerman SF, Rudich Z, Brill S, Shalev H, Shahar G. Longitudinal associations between depression, anxiety, pain, and pain-related disability in chronic pain patients. Psychosom Med 2015;77:333–41.
[23] Rijavec N, Grubic VN. Depression and pain: often together but still a clinical challenge: a review. Psychiat Danub 2012;24:346–52.
[24] Currie SR, Wang J. Chronic back pain and major depression in the general Canadian population. Pain 2004;107: 54–60.
[25] Kiecolt-Glaser JK, Derry HM, Fagundes CP. Inflammation: depression fans the flames and feasts on the heat. Am J Psychiatry 2015;172:1075–91.
[26] Narouze S, Souzdalnitski D. Obesity and chronic pain: systematic review of prevalence and implications for pain practice. Region Anesth Pain Med 2015;40:91–111.
[27] Wang H, Ahrens C, Rief W, Schiltenwolf M. Influence of comorbidity with depression on interdisciplinary therapy: outcomes in patients with chronic low back pain. Arthritis Res Ther 2010;12:R185.
[28] Shi Y, Weingarten TN, Mantilla CB, Hooten WM, Warner DO. Smoking and pain: pathophysiology and clinical implications. Anesthesiology 2010;113:977–92.
[29] Lin CH, Yen YC, Chen MC, Chen CC. Depression and pain impair daily functioning and quality of life in patients with major depressive disorder. J Affect Disorders 2014;166:173–8.
[30] Linton SJ, Bergbom S. Understanding the link between depression and pain. Scand J Pain 2011;2:47–54.

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