Observational Study

Depression Trends in Patients with Chronic Pain: An Analysis of the Nationwide Inpatient Sample

Vwaire Orhurhu, MD[1], Mayowa Olusunmade, MD[2], Yinka Akinola, MD[3], Ivan Urits, MD[1], Mariam Salisu Orhurhu, MD[4], Omar Viswanath, MD[5], Sameer Hirji, MD[6], Alan D. Kaye, MD, PhD[7], Thomas Simopoulos, MD[1], and Jatinder Gill, MD[1]

From: [1]Department of Anesthesiology, Critical Care and Pain, Harvard Medical School, Beth Israel Deaconess Medical Center, Boston, MA; [2]Department of Psychiatry, Rutgers New Jersey Medical School, Newark, NJ; [3]Department of Internal Medicine, Rush Medical Center, Chicago, IL; [4]Departments of Anesthesiology and Critical Care Medicine, Johns Hopkins School of Medicine, Baltimore, MD; [5]Valley Anesthesiology and Pain Consultants, University of Arizona College of Medicine-Phoenix, Phoenix, AZ, and Creighton University School of Medicine, Omaha, NE; [6]Department of Surgery, Brigham and Women's Hospital, Harvard Medical School, Boston, MA; [7]Departments of Anesthesiology and Pharmacology, Louisiana State University School of Medicine, New Orleans, LA

Address Correspondence:
E-Vwaire Orhurhu, MD
Department of Anesthesiology, Critical Care and Pain
Harvard Medical School, Beth Israel Deaconess Medical Center
330 Brookline Ave., FD221A
Boston, MA 02215
E-mail:
vwo569@mail.harvard.edu:

Disclaimer: There was no external funding in the preparation of this manuscript. Conflict of interest: Each author certifies that he or she, or a member of his or her immediate family, has no commercial association (i.e., consultancies, stock ownership, equity interest, patent/licensing arrangements, etc.) that might pose a conflict of interest in connection with the submitted manuscript.

Manuscript received:
12-12-2018
Accepted for publication:
02-27-2019

Free full manuscript:
www.painphysicianjournal.com

Background: Depression remains a major public health issue that affects the lives of many worldwide, including patients with chronic pain. Comorbidities like depression have been associated with decreased quality of sleep, decreased enjoyment of life activities, increased anxiety, and decreased efficacy in treatments among patients with chronic pain. Despite these associations, the trends and demographic characteristics of patients with chronic pain with depression is yet to be investigated.

Objectives: To investigate the trends and demographic characteristics of hospitalized patients with chronic pain with comorbid depression from years 2011 to 2015 in the United States.

Study Design: This was an observational study.

Setting: Patients were identified from a Healthcare Cost and Utilization Project database called National Inpatient Sample (NIS) documentation.

Methods: Patients were identified from the NIS database using International Classification of Diseases, Ninth and Tenth Revision (ICD-9 and ICD-10) diagnosis codes for chronic pain and comorbid depression from years 2011 to 2015.

Results: Between 2011 and 2015, an estimated 9.3 million patients with chronic pain were identified. Of this cohort, 2.2 million patients (22.9%) were diagnosed with comorbid depression. The estimated number of patients with depression varied from 399,865 (22.6%) in 2011 to 421,490 (23.1%) in 2015 ($P = 0.13$). From 2011 to 2015, there was a significant upward trend of depression among blacks (8.1 ± 0.42% to 9.7 ± 0.27%), patients aged 65 to 84 years (29.0 ± 0.39% to 32.4 ± 0.23%), Medicare insured patients (56.1 ± 0.54% to 58.5 ± 0.29%), Medicaid insured patients (14.7 0.4% to 17.1 ± 0.24%), and patients from zip code areas with lowest annual household income (29.2 ± 1.3% to 32.0 ± 0.59%). Among patients with depression, the adjusted total hospitalization cost increased from $43,584 in 2011 to $49,923 in 2015 ($P < 0.001$), with average length of hospital stay stable around 5.05 ± 0.02 days. Most patients were discharged home or with self-care compared with short-term facility (57.9 ± 0.14% vs. 2.0 ± 0.03%).

Limitations: Large database research comes with several limitations. The NIS database does not contain variables that can evaluate disease severity such as depression. In addition, the NIS database is highly dependent on the selection and report accuracy of the appropriate diagnostic ICD codes. These estimates could be imprecise from over or underestimation of the number of patients with chronic pain with comorbid depression.

Conclusions: These findings from the present investigation suggest that depression in patients with chronic pain remained stable from 2011 to 2015, with the majority of patients identified as women, white, and ages 45 to 65 years.

Key words: Chronic pain, depression, National Inpatient Sample

Pain Physician 2019: 22:E487-E494

Chronic pain is a major public health issue that affects the lives of many worldwide and creates significant cost burden to the health care system. In a 2011 study in the United States, chronic pain was found to affect over 100 million adults and incur up to $635 million in costs annually (1). Moreover, an international survey estimated the 12-month prevalence of chronic pain to be 37% in developed countries, and as high as 41% in developing countries (2). It is not surprising, therefore, that pain is one of the leading causes for which patients seek medical care. In many cases, chronic pain may exist in the absence of clear physical pathology. As such, chronic pain is often difficult to understand, to define, to diagnosis, and to treat.

Ultimately, the physical symptoms of chronic pain can impact every aspect of a patient's life and have been shown to correlate with reduced quality of life, decreased enjoyment of life activities, anxiety, and decreased quality of sleep (3). Not surprisingly, as these symptoms are significant components of depression, and chronic pain has been found to be a major factor for depression. In a large international study, patients with chronic pain were 2.3 times as likely to have associated mood disorders (4). In effect, this translates to approximately 20% of individuals with chronic pain to be affected by depression as evidenced in a survey of 46,394 individuals with chronic pain (5). Moreover, in patients seeking treatment at pain medicine institutions, the prevalence of depression can be as high as 50% (6).

Individually, pain and depression are important comorbidities that severely affect patient disability and outcomes. Moreover, the combination of both seems to have a synergistic influence (7). Interestingly, symptoms of pain and depression correlate well and demonstrate a positive association in depression compared with changes in pain scores. Considering this, it is difficult to interpret a causative association, as pain was found to persist despite improvements in symptoms of depression (8). Gaining a better understanding of the association between chronic pain and depression is important and may help lead to improved patient treatment and outcomes. Much of literature that has studied the correlation between chronic pain and depression has been done so via surveys of the general population and in the community setting (9-12). In the present investigation, we assess the rate of comorbid depression and chronic pain in the inpatient population.

Methods

Database Characteristics

National Inpatient Sample (NIS) data from 2010 to 2015 were reviewed and included in our analysis. The NIS is one of the Healthcare Cost and Utilization Projects databases that is sponsored by the Agency for Healthcare Research and Quality (AHRQ) (13). This database is considered the largest all-payer inpatient care database in the United States that has been used in multiple instances to analyze national trends in outcomes, quality, charges, access, and health care use based on data extracted from 7 to 8 million hospital stays.

These hospital stays represent approximately 20% of the US community hospitals, defined as all academic medical centers, general specialty hospitals, nonfederal, and short-term medical centers. The NIS is publicly available and contains no personal identifying information. Therefore, this study was exempt from institutional review board approval. In our analysis, we included chemical dependency treatment facilities, long-term acute care hospitals, short-term rehabilitation facilities, and psychiatric hospitals. Hospitals within a given stratum have similar statistical probability of sample selection regardless of appearance in prior samples. Further information on the design and statistical information of the NIS is available at www.hcup-us.ahrq.gov.

Inclusion and Exclusion Criteria

Our study evaluated patient information data acquired from NIS from 2011 to 2015 to determine the trends of comorbid depression in patients with chronic pain. We included all patients with the diagnosis of depression and chronic pain in our analysis. The International Classification of Diseases, Ninth Revision (ICD-9) codes for patients who had major depression were listed as 300.4, 301.12, 309.0, 309.1, and 311 for 2011 through 2015. Similarly, patients with a diagnosis of chronic pain were listed to have ICD-9 codes of 338.21, 338.22, 338.28, and 338.29 and for fourth quarter of 2015, International Classification of Diseases, Tenth Revision (ICD-10) codes of G89.21, G89.22, G89.28, and G89.29. Patients without a diagnosis of chronic pain were excluded from our analysis.{

Outcomes

For all patients with chronic pain with a diagnosis of major depression from 2011 to 2015, we analyzed patient demographic variables including age, gender, and race. Health care use outcomes such as hospital charges, length of hospital stay, number of inpatient

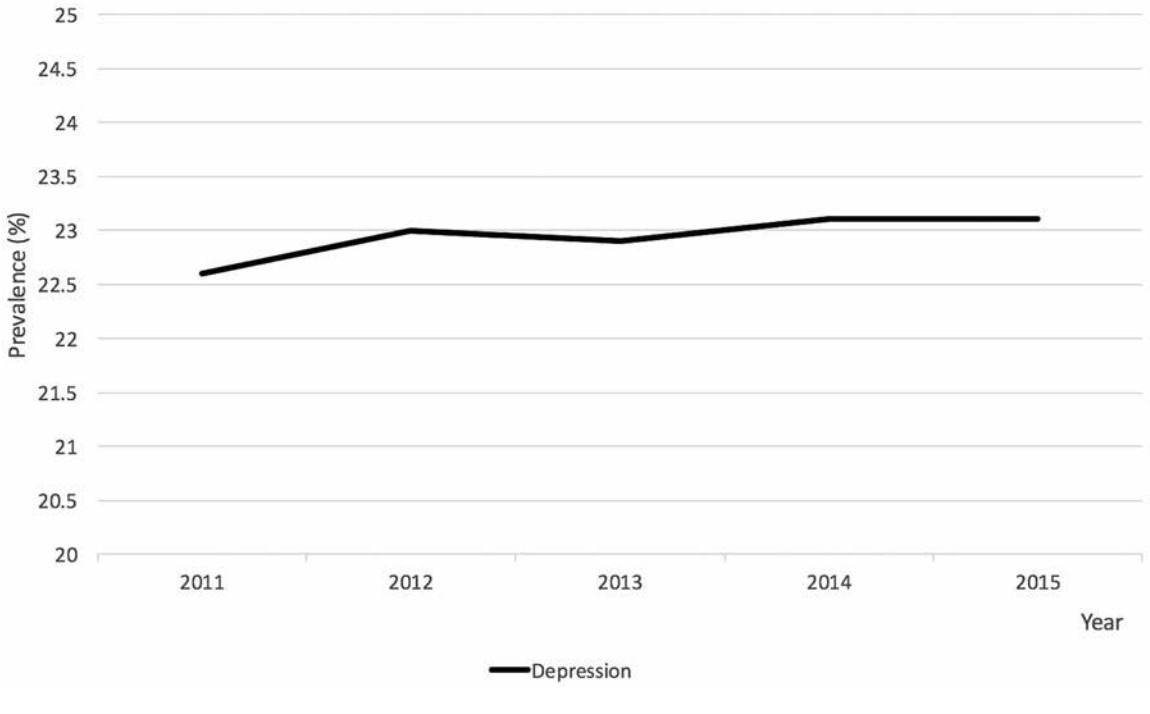

Fig. 1. *Trends in prevalence of comorbid depression among hospitalized patients with chronic pain, 2011-2015.*

procedures, and discharge dispositions were also included in our analysis. The appropriate weights from the NIS database were applied to obtain national estimates.

Statistical Analysis

Our investigation used recommendations from AHRQ to conduct our statistical analysis (13). Appropriate statistical methods were employed for the analysis of survey data. In our descriptive statistics, confirmation of accuracy of our national estimates and variances was accomplished by using survey analytic methods that accounted for stratification and clustering of patients with continuous and categorical variables (14). Survey analytic methods included survey-specific commands (e.g., svymean, svytab, svyregress) for descriptive statistics and trend analyses. The provided trend weights were used to obtain national estimates. Survey-specific linear regression for continuous variable and the Cochran-Armitage test of trend for categorical variable were used for trend analysis. Adjustment for trends in patient characteristics over time was accomplished by using logistic regression model for survey data (svy:regress) and included the year (centered around the mean) as a continuous variable. Analyses were performed using STATA Version 14 (StataCorp, College Station, TX).

Results

Trends of Depression in Patients with Chronic Pain

Between the years 2011 and 2015, approximately 10.3 million patients with chronic pain were identified. Of this cohort, 2.2 million had been diagnosed with depression. The estimated number of patients with depression varied from 399,865 in 2011 to 421,490 in 2015 ($P = 0.13$) (Table 1). The yearly prevalence of depression among patients with chronic pain increased from 22.6% in 2011 to 23.1% in 2015 ($P < 0.001$) (Fig. 1).

Depression Trends and Patient Characteristics

The trends in patient characteristics are displayed in Table 1. The mean (standard error [SE]) age of patients with depression increased from 59.7 (0.19) to 59.5 (0.10) years with the highest proportion of patients ob-

Table 1. *Patient-level characteristics for patients with chronic pain with comorbid depression by calendar year*

Characteristics	Overall	2011	2012	2013	2014	2015	Trend *P*-value
Total patients with depression, Weighted No., n (SE)	2,223,316 (23,611.5)	399,865 (51,620)	433,790 (11,169)	460,520 (11,830)	507,650 (12,991)	421,490 (10,576)	0.13
Patient Characteristics							
Age, year							
Mean (SE), y	59 (.05)	58.7 (.19)	58.5 (.10)	59.0 (.10)	59.3 (.09)	59.5 (.10)	<0.001
<45	16.7 (.1)	17.5 (.35)	17.5 (.2)	16.9 (.19)	16 (.18)	16.0 (.19)	
45 – 64	47.4 (.1)	47.9 (.31)	48.2 (.21)	47.2 (.2)	47.4 (.2)	46.5 (.21)	
65 – 84	30.5 (.11)	29.0 (.39)	29.1 (.23)	30.5 (.23)	31.3 (.22)	32.4 (.23)	
> 84	5.4 (.05)	5.6 (.17)	5.3 (.1)	5.4 (.1)	5.3 (.09)	5.3 (.1)	
Female sex, % (SE)	67.5 (.09)	68.2 (.25)	67.6 (.19)	67.4 (.19)	67.3 (.18)	67.1 (.19)	
Race, % (SE)							
White	83.1 (.2)	84.2 (.69)	83.1 (.45)	83.4 (.38)	82.6 (.39)	82.2 (.39)	0.01a
Black	8.8 (.12)	8.12 (.42)	8.61 (.29)	8.57 (.25)	8.95 (.25)	9.56 (.27)	
Hispanic	5.3 (.13)	5.15 (.5)	5.06 (.24)	5.27 (.26)	5.39 (.25)	5.36 (.24)	
Asian/Pacific Islander	.6 (.03)	.45 (.05)	.54 (.04)	.61 (.05)	.64 (.07)	.74 (.09)	
Native Americans	.74 (.05)	.66 (.17)	.83 (.11)	.74 (.08)	.74 (.08)	.72 (.07)	
Others	1.57 (.07)	1.4 (.19)	1.9 (.23)	1.42 (.09)	1.67 (.12)	1.41 (.11)	
Income quartiles, % (SE)b							
0 – 25	31.0 (.34)	29.2 (1.3)	31.6 (.7)	31.2 (.67)	30.5 (.65)	32.0 (.59)	<0.354c
26 – 50	28.2 (.26)	27.2 (1.01)	27.1 (.48)	29.1 (.47)	30.5 (.47)	26.6 (.42)	
51 – 75	24.0 (.23)	25.2 (.91)	23.8 (.43)	23.7 (.44)	22.8 (.42)	24.6 (.41)	
76 – 100	16.8 (.28)	17.6 (1.1)	17.5 (.54)	16.1 (.53)	16.3 (.51)	16.8 (.52)	
Administrative/Financial Details							
Payment source, % (SE)							
Medicare	57.5 (.15)	56.1 (.54)	56.7 (.29)	57.8 (.29)	58.4 (.29)	58.5 (.29)	<0.001d
Medicaid	15.9 (.12)	14.7 (.4)	15.3 (.21)	15.0 (.21)	16.9 (.24)	17.1 (.24)	
Private insurance	20.1 (.14)	21.4 (.48)	20.6 (.28)	19.9 (.27)	19.3 (.27)	19.3 (.27)	
Elective admissions	20.5 (.18)	20.8 (.69)	20.5 (.36)	20.7 (.34)	20.5 (.32)	20.0 (.32)	0.292
Bed Size, % (SE)e							
Small	15.5 (.29)	12 (.99)	14.2 (.64)	14.2 (.64)	18.6 (.74)	18.1 (.73)	<0.001f
Medium	27 (.41)	24 (1.63)	26.2 (1.04)	26.6 (1.04)	28.7 (1.06)	28.9 (1.03)	
Large	57.5 (.5)	64.1 (1.19)	59.6 (1.19)	59.2 (1.19)	52.7 (1.25)	53 (1.22)	
Teaching hospital, % (SE)	49.9 (.53)	39.6 (2.23)	44.2 (1.33)	45.1 (1.32)	58.8 (1.2)	59.8 (1.16)	<0.001
Hospitals in urban locations	86.4 (.33)	84.7 (1.42)	85.4 (.77)	85.2 (.76)	87.8 (.7)	88.7 (.58)	<0.001

Abbreviations: SE – standard error. OUD – opioid use disorder

a For trends between whites vs others.
b Median household income quartiles based on patient zip code.
c Trend for lowest quartile (0-25th percentile) vs others.
d For Medicare vs others
e Bed size categorization using Agency for Healthcare Research and Quality methods based on number of hospital beds, hospital's location, and teaching status.
f Large vs others, negative trend.

served among patients aged 45 to 64 years. The lowest proportion was observed in elderly patients aged > 84 years. Between the years 2011 and 2015, there was an upward trend of depression among patients within the age group 65 to 84 years. The majority of patients were women and the proportion of women with depression was stable from 2011 to 2015 (68.2 ± 0.25% vs. 67.1 ± 0.19%). Among race, the highest proportion (SE) of patients with depression were white 83.1% (0.20) with the lowest proportion observed in Native Americans 0.74% (0.05). From years 2011 to 2015, the proportion of patients with depression increased from 8.12% (0.42) to 9.56% (0.27) among blacks but decreased from 84.2% (0.69) to 82.2% (0.39) among whites.

Patients within the lowest income quartile (according to zip codes) had the highest proportion of depression diagnosis, 31.0% (0.34), and those within the highest quartile had the lowest proportion of depression, 16.8% (0.28). From years 2011 to 2015, the proportion of depression increased from 29.2% (1.30) to 32.0% (0.59) among the lowest income quartile but decreased from 17.6% (1.10) to 16.8% (0.52) among the highest income quartile. Patients with depression were more commonly insured by Medicare than private insurance (57.5% vs. 20.1%; $P < 0.001$). From years 2011 to 2015, the proportion of depression increased from 56.1% (0.54) to 58.5% (0.29) among Medicare patients but decreased from 21.4% (0.48) to 19.3% (0.27) among private insurance patients. Most patients with chronic pain with depression were admitted at hospitals with large bed size compared with smaller beds (57.5% vs. 15.5%; $P < 0.0001$). From 2011 to 2015, the proportion of depression increased from 12.0% (0.99) to 18.1% (0.73) among small bed size facilities but decreased from 64.1% (1.19) to 53% (1.22) among large bed size hospitals.

Trends of Depression and Health Care Use

After adjusting for inflation, the total hospital cost of patients with depression increased from $43,584 (1,292) in 2011 to $49.923 (719) in 2015 ($P < 0.001$) (Table 2). Similarly, the mean length of hospital stay was stable at 5.03 (0.07) days to 5.11 (0.04) days. The mean number of inpatient procedures was not different across all 5 years ($P = 0.88$). The majority of patients with depression who were discharged to either home or self-care compared with short-term rehabilitative facility was 57.9 ± 0.14% and 2.0 ± 0.03%, respectively.

Discussion

Multiple previous studies have examined the relationship between chronic pain and depression (4,15-17). The majority of studies, however, have been conducted in the outpatient setting, raising the need to address the relationship of these comorbidities in the inpatient setting (17,18). Our study focuses on the relationship between comorbid chronic pain and depression within the inpatient setting, and moreover investigates trends within this association. Our analysis demonstrates a stable trend in the prevalence of major depression in patients with chronic pain over the course of 5 years, with an average of 22.9% of inpatients identified with major depression during their hospital stay during the years 2011 to 2015. Additionally, the number of patients diagnosed with major depression over the course of 5 years was stable and did not demonstrate a progressive increase. The highest recorded number of patients with depression was recorded as 507,650 in 2014.

White patients were found to have the highest pro-

Table 2. *Health care use for depression and patients with chronic pain by calendar year.*

Characteristics	Overall	2011	2012	2013	2014	2015	Trend *P* value
Hospitalization cost, % (SE), 2015 US$	46,267 (350)	43,584 (1,292)	43,521 (636)	46,470 (686)	47,489 (707)	49,923 (719)	0.00
Length of stay, mean (SE), days	5.05 (0.02)	5.03 (0.07)	4.99 (0.03)	5.05 (0.03)	5.04 (0.03)	5.11 (0.04)	0.00
Number of procedures, mean (SE), n	1.54 (0.01)	1.55 (0.04)	1.52 (0.02)	1.56 (0.02)	1.56 (0.02)	1.53 (0.02)	0.88
Hospitalization outcome, % (SE)							
Home or self-care	57.9 (0.14)	59.5 (0.49)	59.4 (0.28)	57.6 (0.29)	56.8 (0.27)	56.3 (0.28)	
Short-term hospital	2 (0.03)	2.0 (0.1)	2.1 (0.07)	2 (0.06)	2.0 (0.06)	2.0 (0.06)	
Skilled care facility	20.6 (0.1)	20.2 (0.32)	20 (0.2)	20.8 (0.19)	20.9 (0.19)	21.1 (0.19)	
Home health care	16.9 (0.1)	15.8 (0.34)	16 (0.2)	16.9 (0.21)	17.6 (0.2)	17.9 (0.22)	

portion of major depression, 83.1%, closely followed by black patients, 8.8%. Our findings are most consistent with Ang et al (19), who similarly reported nonwhite patients to have the highest proportion of depression. This is contrasted, however, by a study that reported no racial correlates to rates of depression in patient populations (20). Interestingly, our findings were further discordant with the findings of Green et al (21), who reported more pain and depressive symptoms in African Americans compared with white Americans. Our study found that the majority of patients with depression were between ages 45 to 64 years, also demonstrating the highest rate at 47%. This is different from the findings of Okifuji et al (3) who observed a stronger association of pain and depression in the older population of 70 years and older. Our findings showed that patients among the age group 65 to 84 years had the second highest rate of depression. In addition, this age group had an increasing trend of depression. Women were found to have a significantly higher proportion of major depression compared with men over the course of the study. The impact of sociodemographic variables and pain-related beliefs on pain-related outcomes for patients with comorbid chronic pain and depression will need to be further studied (19).

It is well established that patients with chronic pain with major depression have a higher health care use cost (6,9,18,22-24). Few studies, however, have investigated the trend of this association. The average hospital length of stay for patients with chronic pain who had comorbid depression was 5.05 days and remained stable from years 2012 to 2014. The average number of procedures performed on patients remained fairly stable over the study period. Our study found that the average health care cost for patients with chronic pain with major depression significantly increased over the 5-year period from 2011 to 2015. This rising trend may reflect the trend of generalized increase in health care costs over the past few years with the advent of technological advancements. This is further reinforced by the fact that the prevalence of depression remained stable over the course of our study. Additional studies are needed to investigate this trend in this population.

There were a dramatically greater number of patients with comorbid depression and pain being discharged to home in favor over supportive rehabilitative facility. This finding suggests that a diagnosis of comorbid depression does not lead to clinically relevant prolonged outpatient recovery or worsened ability to care for oneself. This may be further reinforced by the progressive declined prevalence over the course of our study. We recognize that investigations in this population are scant, and thus further research is needed to delineate our findings.

Limitations

There are several limitations with this study. First, the NIS database does not contain variables that can evaluate disease severity. This information, such as the severity of depression and its relationship to worsening chronic pain and other psychopathologies, was not available for analysis. Second, the NIS database does not include detailed comorbid depression-related cost information. It only reports total hospital charges. This unfortunately limits specific cost analysis such as intensive care unit admission cost, cost of administered anesthesia, procedure room charges, and postoperative charges. Third, health care use outcomes available for analysis in this study may not be directly related to comorbid depression. They could be influenced by multiple factors such as payer status and social factors. Fourth, the NIS database is highly dependent on the selection and report accuracy of the appropriate diagnostic ICD codes (25). For example, the rise in comorbid depression may reflect coding artifact or because of the implementation and rapid adoption of new ICD-9 codes. The patient data analyzed from the NIS may underestimate the number of patients with chronic pain with comorbid depression.

Conclusions

Depression poses a major health concern for patients with chronic pain. This retrospective analysis of NIS data, from 2011 to 2015, demonstrates that patients identified as white, women, and aged 45 to 65 years constitute the largest proportion of affected individuals. White patients also experienced the greatest reduction in depression from 2011 to 2015, which may suggest disparities in treatment availability and targeting. Further, despite relative consistency in patient hospitalization, length of stay, rates of provider interventional procedures, and discharge pathways, costs related to depression grew significantly over this period. With approximately 22.9% of adults with depression, dramatic improvements are needed in the safety of provider practices, patient education, counseling, and depression treatment availability.

Acknowledgments

Author contributions: Dr. Orhurhu and Dr. Olusunmade had full access to all of the data in the study and take responsibility for the integrity of the data and the accuracy of the data analyses.

Study concept and design: Dr. Orhurhu, Dr. Simopoulos, Dr. Jatinder, and Dr. Kaye. Acquisition of data: Dr. Orhurhu and Dr. Olusunmade. Analysis and interpretation of data: Dr. Orhurhu and Dr. Olusunmade. Drafting of the manuscript: Dr. Urits, Dr. Salisu Orhurhu, Dr. Akinola, Dr. Orhurhu, Dr. Viswanath, Dr. Hirji, Dr. Jatinder, and Dr. Kaye. Critical revision of the manuscript for important intellectual content: all authors. Statistical analysis: Dr. Orhurhu, Dr. Akinola, Dr. Olusunmade, and Dr. Salisu Orhurhu. Study supervision: Dr. Orhurhu, Dr. Jatinder, Dr. Simopoulos, and Dr. Kaye.

References

1. Institute of Medicine (US) Committee on Advancing Pain Research, Care, and Education. *Relieving Pain in America: A Blueprint for Transforming Prevention, Care, Education, and Research*. Washington, DC: National Academies Press (US); 2011.
2. Tsang A, Von Korff M, Lee S, Alonso J, Karam E, Angermeyer MC, et al. Common Chronic pain conditions in developed and developing countries: Gender and age differences and comorbidity with depression-anxiety disorders. *J Pain* 2008; 9:883-891.
3. Okifuji A, Turk DC. Chronic pain and depression. In: Flaten M, al'Absi M (eds). *Neuroscience of Pain, Stress, and Emotion*. New York, Elsevier, 2016: pp. 181-201.
4. Demyttenaere K, Bruffaerts R, Lee S, Posada-Villa J, Kovess V, Angermeyer MC, et al. Mental disorders among persons with chronic back or neck pain: Results from the world mental health surveys. *Pain* 2007; 129:332-342.
5. Breivik H, Collett B, Ventafridda V, Cohen R, Gallacher D. Survey of chronic pain in Europe: Prevalence, impact on daily life, and treatment. *Eur J Pain* 2006; 10:287-333.
6. Bair MJ, Robinson RL, Katon W, Kroenke K. Depression and pain comorbidity. *Arch Intern Med* 2003; 163:2433.
7. Mossey JM, Gallagher RM. The longitudinal occurrence and impact of comorbid chronic pain and chronic depression over two years in continuing care retirement community residents. *Pain Med* 2004; 5:335-348.
8. Gerrits MMJG, van Marwijk HWJ, van Oppen P, van der Horst H, Penninx BWJH. Longitudinal association between pain, and depression and anxiety over four years. *J Psychosom Res* 2015; 78:64-70.
9. Arnow BA, Blasey CM, Lee J, Fireman B, Hunkeler EM, Dea R, et al. Relationships among depression, chronic pain, chronic disabling pain, and medical costs. *Psychiatr Serv* 2009; 60:344-350.
10. Outcalt SD, Kroenke K, Krebs EE, Chumbler NR, Wu J, Yu Z, et al. 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; 38:535-543.
11. Stubbs B, Vancampfort D, Veronese N, Thompson T, Fornaro M, Schofield P, et al. Depression and pain: Primary data and meta-analysis among 237 952 people across 47 low- and middle-income countries. *Psychol Med* 2017; 47:2906-2917.
12. Arnow BA, Hunkeler EM, Blasey CM, Lee J, Constantino MJ, Fireman B, et al. Comorbid depression, chronic pain, and disability in primary care. *Psychosom Med* 2006; 68:262-268.
13. Healthcare Cost and Utilization Project (HCUP). Content last reviewed March 2019. Agency for Healthcare Research and Quality, Rockville, MD. www.ahrq.gov/data/hcup/index.html. Accessed October 24th 2018. .
14. Houchens REA. HCUP Method Series Report # 2003-02. US Agency for Healthcare Research and Quality. Final Rep Calc Nationwide Inpatient Sample Variances, 2001. 2005. www.hcup-us.ahrq.gov/reports/methods/2003_02.pdf Accessed October 24th 2018.
15. Gambassi G. Pain and depression: The egg and the chicken story revisited. *Arch Gerontol Geriatr* 2009; 49(Suppl 1):103-112.
16. Bair MJ, Robinson RL, Eckert GJ, Stang PE, Croghan TW, Kroenke K. Impact of pain on depression treatment response in primary care. *Psychosom Med* 2004; 66:17-22.
17. 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; 70:890-897.
18. Beehler GP, Rodrigues AE, Mercurio-Riley D, Dunn AS. Primary care utilization among veterans with chronic musculoskeletal pain: A retrospective chart review. *Pain Med* 2013; 14:1021-1031.
19. 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; 11:482-491.
20. Edwards RR, Doleys DM, Fillingim RB, Lowery D. Ethnic differences in pain tolerance: Clinical implications in a chronic pain population. *Psychosom Med* 2001; 63:316-323.
21. Green CR, Baker TA, Sato Y, Washington TL, Smith EM. Race and chronic pain: A comparative study of young black and white Americans presenting for management. *J Pain* 2003; 4:176-183.
22. Alschuler KN, Otis JD. Coping strategies and beliefs about pain in veterans with comorbid chronic pain and significant levels of posttraumatic stress disorder symptoms. *Eur J Pain* 2012; 16:312-319.
23. 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; 157:1472-1479.

24. Blyth FM, March LM, Brnabic AJM, Cousins MJ. Chronic pain and frequent use of health care. *Pain* 2004; 111:51-58.

25. Berthelsen CL. Evaluation of coding data quality of the HCUP National Inpatient Sample. *Top Health Inf Manage* 2000; 21:10-23.