

# The added burden of depression in patients with osteoarthritis in Japan

This article was published in the following Dove Press journal:  
*ClinicoEconomics and Outcomes Research*

Toshinaga Tsuji<sup>1</sup>  
Ken Nakata<sup>2</sup>  
Jeffrey Vietri<sup>3</sup>  
Dena H Jaffe<sup>4</sup>

<sup>1</sup>Medical Affairs Department, Shionogi & Co., Ltd, Osaka, Japan; <sup>2</sup>Medicine for Sports and Performing Arts, Osaka University, Suita, Japan; <sup>3</sup>Health Outcomes Practice, Health Division, Kantar, 4 Ariel Sharon Street, Horsham, PA, USA; <sup>4</sup>Health Outcomes Practice, Health Division, Kantar, Tel Aviv, Israel

**Objectives:** In Japan, osteoarthritis (OA) is a leading source of pain and disability; depressive disorders may limit patients' ability to cope with OA. This study examined the incremental effect of depression on the relationship between OA and health-related outcomes.

**Methods:** Data from the 2014 Japan National Health and Wellness Survey (N=30,000) were collected on demographics, OA characteristics, and health characteristics of patients with OA. Depression symptoms were measured, and outcomes included health-related quality of life (HRQoL), work productivity and activity impairment, and health care resource utilization. Generalized linear regression models controlling for confounders were used to predict health-related outcomes.

**Results:** Of 565 respondents with OA, 63 (11%) had symptoms of moderate or severe depression. In adjusted models, HRQoL remained lower among respondents with than without depression ( $p<0.001$ ). Higher levels of presenteeism (mean±SE: 50%±9% vs 23%±2%) and activity impairment (mean±SE: 57%±7% vs 30%±1%) were observed for patients with than without depression ( $p<0.001$ ); however, there were no differences for absenteeism ( $p=0.534$ ). Patients with depression (vs no depression) reported more health care provider visits, emergency room visits, and hospitalizations (for all,  $p<0.001$ ).

**Conclusion:** Depression heightens the health-related burden of OA. Greater attention to depression among patients with OA is warranted.

**Keywords:** depression, quality of life, Japan musculoskeletal diseases, osteoarthritis

## Introduction

Osteoarthritis (OA) is the most prevalent form of arthritis in Japan and worldwide.<sup>1–2</sup> In Japan, knee-related OA is found in 43% of men and 62% of women 40 years and older, while shoulder OA affects 17% of patients.<sup>3,4</sup> OA comprises an estimated 75% of arthritis cases; it is one of the 10 leading sources of disability globally and one of the main sources of disability in older age. OA affects over half of the population aged 65 years and older.<sup>5</sup>

OA is caused by mechanical stress and inflammation on the joints resulting in a breakdown of joint cartilage and the underlying bone. Symptoms often include joint pain, swelling, and stiffness, which can further lead to physical limitations and disability, sleep disturbance, and fatigue. OA is not only associated with chronic pain and disability but it is also related to poor mental health, with depressive disorders and anxiety being common among patients with OA.<sup>11,14</sup> Specifically, a systematic review showed that 20% of patients with OA experience depression or anxiety.<sup>11–13</sup> Because the weight-bearing joints (eg, knee, hip, or ankle) tend to be

Correspondence: Dena H Jaffe  
Health Division, Kantar, 4 Ariel Sharon  
Street, Tel Aviv, Israel  
Tel +972 2 993 8496  
Fax +972 2 993 8486  
Email dena.jaffe@kantarhealth.com

most affected, patients with OA may experience restrictions in their ability to perform daily activities, which is associated with depression.<sup>6–8</sup> The relationship between musculoskeletal pain and mental health has also been reported in recent studies from Japan in which more severe chronic lower back pain was associated with lower quality of life and greater health care resource use.<sup>9–13</sup> Overall, the connection between OA and mental health has important implications, as depression has been linked to greater pain sensitivity and poorer coping mechanisms, which can subsequently interfere with the ability to successfully manage OA symptoms.<sup>5,15,16</sup>

OA has been identified as a leading source of pain and disability in Japan.<sup>13</sup> The association between depression and OA and the negative effect of depression on a patient's ability to successfully cope with OA have been well established. However, there is a scarcity of literature on patients with OA in Japan who also experience depression. We hypothesize that in Japan, the incremental effects of depression on patients with OA are represented in the increased health-related burden. This objective was accomplished by documenting differences in patient characteristics, health-related quality of life (HRQoL), and healthcare resource use between patients with OA by the presence of depressive symptoms.

## Methods

### Sample

For this retrospective observational study, data were collected from the 2014 Japan National Health and Wellness Survey (Kantar Health, New York, USA) as reported previously.<sup>9,17</sup> NHWS respondents were recruited through voluntary survey panels, with sampling stratified by gender and age to reflect the demographic distribution of the Japanese general adult population, as reported in the US Census International Database.<sup>18</sup> The 2014 Japan NHWS was reviewed and exempted by Pearl Institutional Review Board (IRB) (Indianapolis, IN, USA; study number 14-KAN-106) on December 1, 2014. The IRB determined this study met the exemption requirements under 45CFR46.101(b)(2). Potential respondents for the NHWS were identified through the Lightspeed Research general panel. A convenience sample was used with an attempt to approximate the age and sex distribution of the adult population in Japan. All respondents who completed the online informed consent form were eligible to complete the survey. No ethical review was undertaken specifically

to the analysis of the anonymous data presented in this report. All data were self-reported and missing data were reported as “declined to answer”. For example, previous studies have shown that the NHWS Japan data are similar in demographic composition to the Japan adult population and that disease-related characteristics for OA and for other conditions were similarly distributed.<sup>19–21</sup> Of the total NHWS sample (N=30,000), 565 respondents reported receiving an OA diagnosis from a physician and were included in the current study.

## Measures

### Depression symptoms

Depression symptoms were measured using the Patient Health Questionnaire (PHQ-9),<sup>22</sup> a validated scale for classifying the severity of depressive symptoms over the last 2 weeks. According to the PHQ-9, depression symptom severity is categorized as scores of 0–4=none, 5–9=mild, 10–14=moderate, 15–19=moderately severe, and 20–27=severe. The scale evaluates the frequency of anhedonia, depressed mood, sleep disturbance, lack of energy, appetite disturbance, negative self-feelings, difficulty concentrating, psychomotor retardation or agitation, and thoughts of self-harm. A single-item measure of the interference of these symptoms was also included. For this study, respondents who scored  $\geq 10$  (the cutoff associated with symptoms of moderate depression) were considered to have exhibited depressive symptoms, regardless of whether they indicated a diagnosis of depression, and respondents scoring  $< 10$  (associated with minimal or mild depression symptoms) were considered not to have symptoms of depression; this value has shown good sensitivity and specificity for major depression in previous research.<sup>22</sup>

### Demographic characteristics

The demographic characteristics assessed included age, gender, marital status (married or living with a partner vs other), employment status (full/part-time vs not employed/disabled/retired/student/homemaker), annual household income ( $< ¥3$  million,  $¥3$ – $< ¥5$  million,  $¥5$ – $< ¥8$  million,  $\geq ¥8$  million, or decline to answer), and level of education (completed 4-year university degree vs less than university degree).

### Health-related characteristics

Health-related characteristics that were assessed included body mass index (calculated from height and weight),

cigarette smoking (never or former vs current), alcohol use (any vs no alcohol), and vigorous exercise in the past month (yes vs no). Charlson Comorbidity Index (CCI) scores were also included. The CCI is a summary weighted index of the presence of the following conditions: HIV/AIDS, metastatic tumor, moderate or severe liver disease, lymphoma, leukemia, any tumor, moderate/severe renal disease, hemiplegia, diabetes, mild liver disease, ulcer disease, connective tissue disease, chronic pulmonary disease, dementia, cerebrovascular disease, peripheral vascular disease, myocardial infarction, congestive heart failure, and diabetes with end organ damage.<sup>23</sup> The greater the total index score, the greater the comorbid burden on the patient. CCI was used in this study as a categorical variable (0, 1, 2+).

### OA-related characteristics

Measures of OA-related characteristics included self-reported length of diagnosis (in years), number of joints affected, severity of arthritis (mild, moderate, or severe), frequency of problems with arthritis (daily, 4–6 times a week, 2–3 times a week, once a week, 2–3 times a month, or once a month or less often), and use of prescription medication for arthritis (yes vs no).<sup>17</sup>

### Health-related quality of life

HRQoL was assessed with the revised validated Medical Outcomes Study 36-Item Short Form Health Survey version 2 (SF-36v2). The instrument contains 36 questions and measures eight health concepts (physical functioning, role physical, bodily pain, general health, vitality, social functioning, role emotional, and mental health), according to Japanese-based population norms (mean=50, SD=10). Mental component summary and physical component summary scores with US-based norms (mean=50, SD=10) were also used. In addition, the SF-36v2 instrument was used to generate a single index of health state utilities, namely the Short-Form 6-Dimension (SF-6D).<sup>24</sup> Scoring of the SF-6D takes into consideration six dimension of the SF-36, including physical functioning, role participation, social functioning, bodily pain, mental health, and vitality. It is scored. The SF-6D index has interval scoring properties and yields summary scores from 0.0 (worst health state) to 1.0 (best health state) with an empirical floor of 0.3. Higher scores on these measures indicate better HRQoL.

### Work productivity and activity impairment

Work productivity and activity impairment was measured using the validated Work Productivity and Activity

Impairment-General Health questionnaire,<sup>25</sup> which measures four domains: 1) absenteeism (the percentage of work time missed within the past week due to one's health), 2) presenteeism (the percentage of impairment at work within the past week due to one's health), 3) overall work productivity loss (an overall impairment estimate that assesses a combination of absenteeism and presenteeism), and 4) activity impairment (the percentage of impairment in day-to-day activities within the past week due to one's health). Higher percentage scores indicate greater impairment. Only employed participants provided data for absenteeism, presenteeism, and overall work productivity impairment, whereas the full sample of patients with OA completed the activity impairment measure.

### Health care resource use

Health care resource use was measured using self-reported number of total physician visits, emergency room (ER) visits, number of ER visits, and the number of times respondents were hospitalized in the past six months.

### Analyses

Respondents with OA and moderate to severe depression symptoms (PHQ-9 score  $\geq 10$ ) were compared to respondents with physician-diagnosed OA and mild or no depression symptoms using chi-square tests for categorical variables and independent-samples t-tests for continuous variables. Multivariable models analyzed health outcomes as a function of depression symptoms (reference=none/mild depression vs depression=moderate/severe). These models were used to demonstrate the burden of depression symptoms on patients with physician-diagnosed OA, controlling for socio-demographic or health-related variables that varied by group at  $p < 0.05$  in the bivariate analyses: age, marital status, employment status, and smoking status. Regression models were chosen according to the distribution of the outcome variable as tested using the one-sample Kolmogorov–Smirnov test for normality and for non-linear outcomes using the likelihood ratio test in the regression model to assess over-dispersion (Poisson vs negative binomial). Thus, generalized linear regression models were used for measures with normal (HRQoL and work productivity outcomes) or negative binomial (health care resource utilization) distributions. Linear model assumptions were tested for linearity of covariates and disproportionate influential observations using Cook's distance and studentized residuals. All analyses assumed a null hypothesis, with a two-sided  $\alpha < 0.05$ , and were

conducted with IBM Statistical Package for the Social Sciences (SPSS) Statistics, version 22 or later.

## Results

Our final sample comprises a total of  $N=565$  respondents with OA, and 63 (11%) of these individuals had moderate or severe depression symptoms, as measured by the PHQ-9 (score  $\geq 10$ ). These individuals were considerably younger than those without depression symptoms, more likely to be employed, less likely to be married or living with a partner, had higher CCI scores, and were more often current smokers, although gender and OA-related characteristics did not differ significantly between patients with and without depression symptoms (Table 1).

Depression symptoms were associated with substantial decrements in HRQoL (Table 2), particularly on the MCS (nearly 20 points) and SF-6D (over 0.15 points). Substantial and significant decrements on all other SF-36v2 metrics, including physically oriented metrics, such as PCS, physical functioning, and bodily pain, were also observed.

Among employed respondents, moderate to severe depression symptoms were associated with markedly higher work productivity impairment, except for absenteeism (Table 3). For patients with moderate to severe depression symptoms, both presenteeism and overall work impairment were approximately double the levels reported by their counterparts with no or mild depression symptoms. Activity impairment was also nearly double for those with moderate to severe depression symptoms, relative to the group with no or mild depression symptoms. Moderate to severe depression symptoms were associated with a greater number of physician visits, ER visits, and hospitalizations for patients with OA, compared with no or mild depression symptoms (Table 3).

After adjusting for potential confounders, HRQoL remained significantly lower among respondents with moderate to severe depression symptoms, compared with those with no or mild depression symptoms (Table 4). Additionally, impairments to work productivity (presenteeism and overall work impairment) and daily activities, as well as health care resource utilization (physician visits, ER visits, and hospitalizations), were significantly higher among respondents with moderate to severe (vs mild or no) depression symptoms. For absenteeism, no statistically significant differences were observed (Table 4).

## Discussion

Approximately 11% of respondents with OA in our study had symptoms of moderate to severe depression, according

to the PHQ-9. Our results showed that depression symptoms are more severe among patients with OA who smoke and are not married or living with a partner. The frequency of moderate to severe depression among employed patients with OA was greater than among the unemployed. The reason could be that the age of patients with symptoms of moderate to severe depression was, on average, lower than that of patients with no or mild depression symptoms, and patients under age 60 had a higher frequency of employment. Gender was not differentially associated with depression severity in OA, which may be due to cultural factors and may also warrant further investigation in a future study.

The prevalence of moderate to severe depression symptoms reported by the current study is lower than the estimates reported in US-based studies investigating OA and depression.<sup>16,26</sup> This 11% prevalence of depression may reflect a slight skew toward a younger healthier population in the NHWS in general.<sup>27</sup> Cultural factors may play a role, as depression is less prevalent in Japan than in Western countries.<sup>28</sup> Results were consistent with other research that identified characteristics, such as smoking,<sup>29,30</sup> living alone,<sup>16</sup> and widowed or divorced status,<sup>29</sup> as being associated with depression. However, it is unclear whether these characteristics are causal factors for depression in the adult population with OA, and further research is needed to clarify this issue.

Respondents with OA who had symptoms of moderate to severe depression had worse mental and physical HRQoL, including more interference from bodily pain, than those with no or mild depression symptoms, even after adjusting for potential confounders. Studies show the interconnectedness between physical pain and mental health.<sup>5,16,31–34</sup> While depression and anxiety are associated with reduced activity leading to chronic pain, functional disability has been reported to be a risk factor for depression, both pathways impacting prognosis and rehabilitation.<sup>31–34</sup>

The literature has produced conflicting results as to whether the relationship between depression and pain or disability varies by gender.<sup>9,15,31</sup> Specifically, some studies have reported significant gender differences in depression among those with OA, with women reporting higher rates of depression than men.<sup>15</sup> In contrast, the findings that reported no significant gender difference in the prevalence of depression severity in participants with OA are aligned with other studies.<sup>15,31</sup>

**Table 1** Respondent characteristics for patients with OA with and without depression

	Total (N=565)		No or mild depression (N=502)		Moderate or severe depression (N=63)		p-value
	%/Mean	n/SD	%/Mean	n/SD	%/Mean	n/SD	
Age, mean (SD) years	59.1 (12.1)		60.6 (11.0)		47.0 (13.7)		<0.001
<40 years	8.8%	50	6.4%	32	28.6%	18	<0.001
40–49 years	8.3%	47	6.0%	30	27.0%	17	
50–59 years	24.6%	139	24.7%	124	23.8%	15	
60–69 years	45.1%	255	48.4%	243	19.0%	12	
70+ years	13.1%	74	14.5%	73	1.6%	1	
Female	58.6%	331	58.6%	294	58.7%	37	0.980
Married or living with partner	73.3%	414	74.9%	376	60.3%	38	0.014
Employed full or part-time	45.3%	256	43.2%	217	61.9%	39	0.005
Annual household income							0.300
<¥3 million	18.4%	104	17.5%	88	25.4%	16	
¥3 million to <¥5 million	27.6%	156	27.5%	138	28.6%	18	
¥5 million to <¥9 million	29.7%	168	31.1%	156	19.0%	12	
¥9 million or more	13.8%	78	13.5%	68	15.9%	10	
Decline to answer	10.4%	59	10.4%	52	11.1%	7	
Completed 4-year university degree	43.5%	246	42.6%	214	50.8%	32	0.218
CCI							0.053
0	69.9%	395	70.5%	354	65.1%	41	
1	20.9%	118	21.3%	107	17.5%	11	
2+	9.2%	52	8.2%	41	17.4%	11	
BMI categories in kg/m <sup>2</sup>							0.157
Underweight (<18.5)	7.6%	43	7.2%	36	11.1%	7	
Normal (18.5–24.9)	63.4%	358	65.1%	327	49.2%	31	
Overweight (25–29.9)	21.8%	123	20.7%	104	30.2%	19	
Obese (≥30)	4.4%	25	4.4%	22	4.8%	3	
Decline to answer	2.8%	16	2.6%	13	4.8%	3	
Smoking status							0.012
Current smoker	17.3%	98	15.7%	79	30.2%	19	
Former smoker	31.3%	177	32.5%	163	22.2%	14	
Never smoker	51.3%	290	51.8%	260	47.6%	30	
Drinks alcohol	67.4%	381	66.1%	332	77.8%	49	0.063
Vigorous exercise in past month	49.7%	281	50.4%	253	44.4%	28	0.373

(Continued)

**Table 1** (Continued).

	Total (N=565)		No or mild depression (N=502)		Moderate or severe depression (N=63)		p-value
	%/Mean	n/SD	%/Mean	n/SD	%/Mean	n/SD	
Length of arthritis diagnosis, mean (SD) years	9.5 (11.8)		9.7 (12.1)		7.6 (8.9)		0.221
Number of joints affected, mean (SD)	1.8 (1.6)		1.8 (1.5)		2.0 (2.1)		0.239
Severity of arthritis (self-reported)							
Mild	50.1%	283	50.4%	253	47.6%	30	0.514
Moderate	38.4%	217	38.6%	194	36.5%	23	
Severe	11.5%	65	11.0%	55	15.9%	10	
Frequency of problems with arthritis							0.406
Daily	36.3%	205	36.3%	182	36.5%	23	
4–6 times a week	8.1%	46	8.2%	41	7.9%	5	
2–3 times a week	12.2%	69	11.6%	58	17.5%	11	
Once a week	4.4%	25	4.0%	20	7.9%	5	
2–3 times a month	11.0%	62	11.2%	56	9.5%	6	
Once a month or less often	28.0%	158	28.9%	145	20.6%	13	0.105
Use a prescription for OA	30.8%	174	29.7%	149	39.7%	25	

**Abbreviations:** BMI, body mass index; CC, Charlson Comorbidity Index; OA, osteoarthritis; SD, standard deviation.

**Table 2** Health-related quality of life for patients with OA with and without depression<sup>a</sup>

	Total (N=565)		No or mild depression (N=502)		Moderate or severe depression (N=63)		p-value
	Mean	(SD)	Mean	(SD)	Mean	(SD)	
MCS	47.6	(10.7)	49.7	(8.7)	30.7	(10.6)	<0.001
PCS	46.9	(7.8)	47.4	(7.4)	42.6	(9.7)	<0.001
SF-6D	0.69	(0.12)	0.71	(0.11)	0.54	(0.11)	<0.001
Physical functioning	42.8	(15.9)	43.9	(14.4)	33.3	(22.6)	<0.001
Physical role limitations	43.3	(13.7)	44.9	(12.4)	30.4	(16.7)	<0.001
Bodily pain	42.9	(10.2)	43.9	(9.5)	34.9	(11.7)	<0.001
General health	42.4	(10.8)	43.8	(9.9)	30.9	(10.7)	<0.001
Vitality	45.3	(11.0)	47.1	(9.8)	31.1	(10.4)	<0.001
Social functioning	45.6	(12.9)	47.6	(11.2)	29.4	(14.7)	<0.001
Emotional role limitations	46.0	(12.6)	47.7	(10.9)	31.7	(15.6)	<0.001
Mental health	47.8	(11.1)	50.0	(9.0)	30.3	(10.9)	<0.001

**Notes:** <sup>a</sup>Data are from the self-reported patient survey responses to the Medical Outcomes Study 36-Item Short Form Health Survey version 2 (SF-36v2). Component scores, MCS and PCS, as well as domain scores range from 0-100, with a mean=50 and standard deviation=10, with higher scores indicating better quality of life. The SF-6D is a health utility score ranging from 0.0 (worst health state) to 1.0 (best health state).

**Abbreviations:** MCS, Mental Component Summary; PCS, Physical Component Summary; SD, standard deviation; SF-6D, Short-Form 6-Dimensions.

Greater impairments to work productivity and daily activities among those with than without depression symptoms were reported by a previous study of patients with chronic lower back pain in Japan,<sup>9</sup> which is similar to the results of the current study. Moreover, consistent with the present study, a prior retrospective observational study of 167,068 US patients with arthritis demonstrated that those with (vs without) comorbid depression had greater disability and limitations to work and social activities, as well as poorer general health and HRQoL.<sup>35</sup> Therefore, the collective evidence suggests that depression symptoms may substantially augment the burden of OA.

In the present findings, absenteeism and depression symptoms were not significantly associated with each other, which was aligned with prior research showing Japanese workers tend to have fewer sick leave claims than workers in other countries.<sup>36</sup> Prior research has also reported that health care expenditures were 39% higher among adults with OA who also reported depression, when compared with individuals with OA who did not have depression;<sup>26</sup> this is in accordance with the patterns of health care resource use found in the present study. One possible explanation is that patients with both chronic physical and psychological conditions may use the health-care system more often than individuals who solely have physical impairments.<sup>26</sup> For example, patients with OA who also have symptoms of moderate to severe depression may visit both psychiatric and orthopedic health care providers; alternatively, these patients may perceive their health to be worse, relative to the health perceptions of patients without depression.<sup>26</sup>

Overall, this study contributes to the literature by identifying key differences between respondents with OA who have symptoms of moderate to severe depression and counterparts with no or mild depression symptoms. Notably, this is one of the first studies to explore these relationships among patients with OA in Japan. The observed association between moderate to severe depression symptoms and health-related burden among patients with OA suggests that physicians should screen for and address symptoms of depression when treating OA, particularly for individuals who may be at a greater risk of developing depression. In the workplace, for example, those with presenteeism may be at greater risk of depression, although this may not be the case among those with absenteeism. Mitigating the impact of depression symptoms is essential, as prior research indicates that depression can interfere with the effective management of OA by reducing patients' adherence to their medication regimen.<sup>37</sup> Critical aspects of

**Table 3** Work productivity and activity impairment and health care resource use for patients with OA with and without depression

	Total (N=565)		No or mild depression (N=502)		Moderate or severe depression (N=63)		p-value
	Mean	SD	Mean	SD	Mean	SD	
Work productivity and activity impairment <sup>a</sup>							
Absenteeism (%) <sup>b</sup>	3.8	15.8	3.5	15.4	5.5	17.6	0.472
Presenteeism (%) <sup>c</sup>	27.0	26.8	22.9	24.3	51.5	27.9	<0.001
Overall work impairment (%) <sup>b</sup>	29.2	29.0	24.8	27.0	53.6	28.3	<0.001
Activity impairment (%)	32.5	28.8	29.6	27.3	56.2	29.3	<0.001
Health care resource utilization <sup>d</sup>							
Physician visits (median, IQR)	11.9	16.4	10.7 (7)	13.6 (3–14)	21.3 (12)	29.5 (5–23)	<0.001
ER visits (median, IQR)	0.6	4.9	0.3 (0)	2.1 (0–0)	3.0 (0)	13.4 (0–0)	0.001 <sup>e</sup>
Hospitalizations (median, IQR)	1.6	7.4	1.3 (0)	5.6 (0–0)	4.3 (0)	15.7 (0–0)	0.182 <sup>e</sup>
			(0)	(0–0)	(0)	(0–0)	0.002
							0.082 <sup>e</sup>

**Notes:** <sup>a</sup>The work and activity impairment scale is a patient-reported outcomes questionnaire that examines used to examine work and activity-related impairment in the past week due to one's health. Higher percentage scores indicates greater impairment; <sup>b</sup>Among employed respondents only: total=229; no/mild=194; moderate/severe=35; <sup>c</sup>Among employed respondents only: total=233; no/mild=199; moderate/severe=34; <sup>d</sup>Self-reported total number of healthcare visits or hospitalization days for all health-related issues in the past 6 months was examined for all respondents; <sup>e</sup>Mann-Whitney U test of difference in median values.

**Abbreviations:** ER, emergency room; HCP, healthcare provider; IQR, interquartile range; SD, standard deviation.



**Table 4** Adjusted means of health outcomes for patients with OA with and without depression

	No or mild depression		Moderate or severe depression		p-value
	Mean	(SE)	Mean	(SE)	
HRQoL	(N=502)		(N=63)		
MCS	48.94	(0.48)	31.72	(1.20)	<0.001
PCS	46.94	(0.42)	41.93	(1.04)	<0.001
SF-6D	0.71	(0.01)	0.54	(0.02)	<0.001
Physical functioning	43.14	(0.84)	32.10	(2.08)	<0.001
Physical role limitations	44.46	(0.71)	30.08	(1.75)	<0.001
Bodily pain	43.33	(0.53)	35.01	(1.32)	<0.001
General health	42.55	(0.54)	30.12	(1.33)	<0.001
Vitality	46.21	(0.53)	32.08	(1.31)	<0.001
Social functioning	46.76	(0.63)	29.79	(1.56)	<0.001
Emotional role limitations	47.17	(0.63)	31.84	(1.55)	<0.001
Mental health	49.14	(0.49)	31.25	(1.22)	<0.001
Work productivity and activity impairment (%)	(N=194)		(N=35)		
Absenteeism	3.71	(1.24)	5.15	(2.79)	0.639
Presenteeism	23.14	(1.90)	50.55	(4.45)	<0.001
Overall work impairment	25.01	(2.14)	52.71	(4.81)	<0.001
Activity impairment	(N=502)		(N=63)		
Activity impairment	30.65	(1.49)	56.98	(3.70)	<0.001
Healthcare resource utilization	(N=502)		(N=63)		
Physician visits	11.79	(0.68)	21.69	(3.10)	<0.001
ER visits	0.31	(0.03)	3.12	(0.52)	<0.001
Hospitalizations	1.39	(0.10)	5.15	(0.88)	<0.001

**Notes:** <sup>a</sup>Generalized linear regression models were used for measures with normal distributions (HRQoL and work productivity outcomes) and negative binomial models were run for non-negative count data (healthcare resource utilization). All models were adjusted for age, marital status, employment status, and smoking status that were significant predictors of depression severity at p<0.05 in the bivariate comparisons. Adjusted mean values and standard errors for each outcome are presented at the mean the group variable (none/mild or moderate/severe depression) controlling for each of the covariates. Differences between group mean values (i.e., differences in the indicator variable in the regression model) are indicated using the p-value.

**Abbreviations:** ER, emergency room; HRQoL, health-related quality of life; MCS, Mental Component Summary; SE, standard error; SF-6D, Short-Form 6-Dimensions.

integrated programs that address both depression and OA include screening for depression and pain at the first visit and follow-up, supporting patient self-efficacy through education and behavioral therapy, and adjusting treatment intensity, based on a patient's progress. The results of the current study can help to inform clinicians about the importance of identifying and treating patients with OA who are also likely to concurrently have depression.

The cross-sectional study design prevents us from detecting causal or longitudinal relationships between variables. The measures in the study were self-reported, and respondent recall bias may have introduced measurement error into the study findings. We also cannot exclude the possibility that unmeasured variables could at least partially explain the results, such as clinical measures of severity. The data were collected using an Internet survey of respondents who opted to participate. Therefore, selection bias may have affected the representativeness of the study population and prevalence of OA. Specifically, it is possible that younger adults are more likely to participate in Internet surveys like the NHWS, which could account for the unexpectedly low prevalence of OA in the overall NHWS sample. In general, OA knee prevalence, for example, is highest among older adults ages 70 years and older, and this age group represents approximately 14% of the study sample.<sup>3,4,38</sup> Moreover, given the relatively young age of patients with physician-diagnosed OA in this study, the findings may underestimate both the burden of OA and the incremental impact of depression on this burden.

## Conclusion

In this study, over 10% of patients with physician-diagnosed OA reported symptoms of moderate to severe depression. There were significant differences in HRQoL, work productivity impairment, and health care resource utilization between those with and without moderate to severe depression, even after adjusting for potential confounders. Hence, results suggest that depression may incrementally increase the health-related burden of OA. To help mitigate this burden, physicians should address symptoms of depression when treating patients with OA.

## Acknowledgments

The authors acknowledge Martine C Maculaitis, PhD, for providing editing assistance on behalf of Kantar Health, with funding from Shionogi & Co., Ltd.

## Disclosure

Dr Tsuji is a full-time employee of Shionogi & Co., Ltd. and a stockholder of Shionogi & Co., Ltd. and Takeda Pharmaceutical Company Ltd. Dr Vietri was and Dr Jaffe is a full-time employee of Kantar; Kantar received support from Shionogi & Co., Ltd. for survey access, analysis and the manuscript preparation. Dr Nakata has no conflicts of interest in this work.

## References

- Lawrence RC, Felson DT, Helmick CG, et al. Estimates of the prevalence of arthritis and other rheumatic conditions in the United States: part II. *Arthritis Rheum.* 2008;58(1):26–35. doi:10.1002/art.23176
- Litwic A, Edwards MH, Dennison EM, Cooper C. Epidemiology and burden of osteoarthritis. *Br Med Bull.* 2013;105(1):185–199. doi:10.1093/bmb/lds038
- Yoshimura N, Muraki S, Oka H, Kawaguchi H, Nakamura K, Akune T. Association of knee osteoarthritis with the accumulation of metabolic risk factors such as overweight, hypertension, dyslipidemia, and impaired glucose tolerance in Japanese men and women: the ROAD study. *J Rheumatol.* 2011;38(5):921–930. doi:10.3899/jrheum.100569
- Kobayashi T, Takagishi K, Shitara H, et al. Prevalence of and risk factors for shoulder osteoarthritis in Japanese middle-aged and elderly populations. *J Shoulder Elb Surg.* 2014;23(5):613–619. doi:10.1016/j.jse.2013.11.031
- Hawker GA, Gignac MAM, Badley E, et al. A longitudinal study to explain the pain-depression link in older adults with osteoarthritis. *Arthritis Care Res (Hoboken).* 2011;63(10):1382–1390. doi:10.1002/acr.20298
- Kondo K, Jingushi S, Ohfuji S, et al. Factors associated with functional limitations in the daily living activities of Japanese hip osteoarthritis patients. *Int J Rheum Dis.* 2017;20:1372–1382.
- Sliepen M, Mauricio E, Lipperts M, Grimm B, Rosenbaum D. Objective assessment of physical activity and sedentary behaviour in knee osteoarthritis patients – beyond daily steps and total sedentary time. *BMC Musculoskelet Disord.* 2018;19(1):64. doi:10.1186/s12891-018-1980-3
- Mesci E, Icagasioglu A, Mesci N, Turgut ST. Relation of physical activity level with quality of life, sleep and depression in patients with knee osteoarthritis. *North Clin Istanbul.* 2015;2(3):215–221.
- Tsuji T, Matsudaira K, Sato H, Vietri J. The impact of depression among chronic lower back pain patients in Japan. *BMC Musculoskelet Disord.* 2016;17:447. doi:10.1186/s12891-016-1134-4
- Montgomery W, Vietri J, Shi J, et al. The relationship between pain severity and patient-reported outcomes among patients with chronic low back pain in Japan. *J Pain Res.* 2016;9:337–344. doi:10.2147/JPR.S102063
- Stubbs B, Aluko Y, Myint PK, Smith T. Prevalence of depressive symptoms and anxiety in osteoarthritis: a systematic review and meta-analysis. *Age Ageing.* 2016;45:228–235. doi:10.1093/ageing/afw001
- Ferreira AH, Gomes Godoy PB, de Oliveira NRC, et al. Investigation of depression, anxiety and quality of life in patients with knee osteoarthritis: a comparative study. *Rev Bras Reumatol.* 2015;55(5):434–438. doi:10.1016/j.rbr.2015.03.001
- Hashikawa T, Osaki M, Ye Z, et al. Factors associated with radiographic osteoarthritis of the knee among community-dwelling Japanese women: the Hizen-Oshima Study. *J Orthop Sci.* 2011;16(1):51–55. doi:10.1007/s00776-010-0013-3

14. Wong LY, Yiu RL, Chiu CK, et al. Prevalence of psychiatric morbidity in chinese subjects with knee osteoarthritis in a Hong Kong orthopaedic clinic. *East Asian Arch Psychiatry*. 2015;25(4):150–158.
15. Rosemann T, Backenstrass M, Joest K, Rosemann A, Szecsenyi J, Laux G. Predictors of depression in a sample of 1,021 primary care patients with osteoarthritis. *Arthritis Care Res*. 2007;57(3):415–422. doi:10.1002/art.22624
16. Sale JE, Gignac M, Hawker G. The relationship between disease symptoms, life events, coping and treatment, and depression among older adults with osteoarthritis. *J Rheumatol*. 2008;35(0315–162X (Print)):335–342.
17. Nakata K, Tsuji T, Vietri J, Jaffe DH. Work impairment, osteoarthritis, and health-related quality of life among employees in Japan. *Health Qual Life Outcomes*. 2018;16(1):1–11. doi:10.1186/s12955-017-0829-z
18. US Census Bureau. US Census International Database. Mid-Year Population by Single Year Age Groups - Custom Region - Japan; 2014.
19. Liu GG, daCosta DiBonaventura M, Yuan Y, et al. The burden of illness for patients with viral hepatitis C: evidence from a national survey in Japan. *Value Heal*. 2012;15(1):S65–S71. doi:10.1016/j.jval.2011.11.012
20. Koretsune Y, Rossi B, Iwamoto K, Wang ECY, Dibonaventura M, Briere J. Characteristics, treatment patterns, and unmet needs of Japanese patients with atrial fibrillation. *Res Reports Clin Cardiol*. 2013;4:97–105.
21. Sato M, Vietri J, Flynn JA, Fujiwara S. Treatment for osteoporosis among women in Japan: associations with patient characteristics and patient-reported outcomes in the 2008–2011 Japan national health and wellness surveys. *J Osteoporos*. 2014;2014:1–9. doi:10.1155/2014/909153
22. Kroenke K, Spitzer RL, Williams JBW. The PHQ-9: validity of a brief depression severity measure. *J Gen Intern Med*. 2001;16(9):606–613.
23. Charlson ME, Pompei P, Ales KL, MacKenzie CR. A new method of classifying prognostic comorbidity in longitudinal studies: development and validation. *J Chronic Dis*. 1987;40(5):373–383.
24. Brazier J, Roberts J, Deverill M. The estimation of a preference-based measure of health from the SF-36. *J Health Econ*. 2002;21(2):271–292.
25. Reilly MC, Zbrozek AS, Dukes EM. The validity and reproducibility of a work productivity and activity impairment instrument. *Pharmacoeconomics*. 1993;4(5):353–365. doi:10.2165/00019053-199304050-00006
26. Agarwal P, Sambamoorthi U. Healthcare expenditures associated with depression among individuals with osteoarthritis: post-regression linear decomposition approach. *J Gen Intern Med*. 2015;30(12):1803–1811. doi:10.1007/s11606-015-3393-4
27. Strader C, Goren A, DiBonaventura M. Prevalence of combinations of diabetes complications across NHANES and NHWS. 32nd International Conference on Pharmacoepidemiology & Therapeutic Risk Management (ICPE); Dublin, Ireland; 2016.
28. Ishikawa H, Kawakami N, Kessler RC. World Mental Health Japan Survey Collaborators. Lifetime and 12-month prevalence, severity and unmet need for treatment of common mental disorders in Japan: results from the final dataset of World Mental Health Japan Survey. *Epidemiol Psychiatr Sci*. 2016;25(03):217–229. doi:10.1017/S2045796015000566
29. Dunlop DD, Lyons JS, Manheim LM, Song J, Chang RW. Arthritis and heart disease as risk factors for major depression: the role of functional limitation. *Med Care*. 2004;42(6):502–511.
30. Jeuring HW, Huisman M, Comijs HC, Stek ML, Beekman ATF. The long-term outcome of subthreshold depression in later life. *Psychol Med*. 2016;46(13):1–11.
31. Parmelee PA, Harralson TL, McPherron JA, DeCoster J, Schumacher HR. Pain, disability, and depression in osteoarthritis: effects of race and sex. *J Aging Health*. 2012;24(1):168–187. doi:10.1177/0898264311410425
32. Calvo-Lobo C, Manuel Vilar Fernández J, Becerro-De-Bengoa-Vallejo R, et al. Relationship of depression in participants with nonspecific acute or subacute low back pain and no-pain by age distribution. *J Pain Res*. 2017;10:129.
33. Scopaz KA, Piva SR, Wisniewski S, Fitzgerald GK. Relationships of fear, anxiety, and depression with physical function in patients with knee osteoarthritis. *Arch Phys Med Rehabil*. 2009;90(11):1866–1873. doi:10.1016/j.apmr.2009.06.012
34. Sharma A, Kudesia P, Shi Q, Gandhi R. Anxiety and depression in patients with osteoarthritis: impact and management challenges. *Open access Rheumatol*. 2016; 8:103. doi:10.2147/OARRR.S93516
35. Joshi N, Khanna R, Shah RM. Relationship between depression and physical activity, disability, burden, and health-related quality of life among patients with arthritis. *Popul Health Manag*. 2015;18(2):104–114. doi:10.1089/pop.2014.0062
36. Matsudaira K, Palmer KT, Reading I, Hirai M, Yoshimura N, Coggon D. Prevalence and correlates of regional pain and associated disability in Japanese workers. *Occup Environ Med*. 2011;68(3):191–196. doi:10.1136/oem.2009.053645
37. Depression LE. Osteoarthritis. *Am J Med*. 2008;121:S16–S19. doi:10.1016/j.amjmed.2008.09.009
38. Allen KD, Golightly YM, Hill C, et al. Estimates of the prevalence of arthritis and other rheumatic conditions in the United States. Part I. *Osteoarthr Cartil*. 2012;68(1):S18–S21.

## ClinicoEconomics and Outcomes Research

Dovepress

### Publish your work in this journal

ClinicoEconomics and Outcomes Research is an international, peer-reviewed open-access journal focusing on Health Technology Assessment, Pharmacoeconomics and Outcomes Research in the areas of diagnosis, medical devices, and clinical, surgical and pharmacological intervention. The economic impact of health policy and health systems

organization also constitute important areas of coverage. The manuscript management system is completely online and includes a very quick and fair peer-review system, which is all easy to use. Visit <http://www.dovepress.com/testimonials.php> to read real quotes from published authors.

Submit your manuscript here: <https://www.dovepress.com/clinicoeconomics-and-outcomes-research-journal>