

# The Health-Related Quality of Life, Work Productivity, Healthcare Resource Utilization, and Economic Burden Associated with Levels of Suicidal Ideation Among Patients Self-Reporting Moderately Severe or Severe Major Depressive Disorder in a National Survey

This article was published in the following Dove Press journal:  
*Neuropsychiatric Disease and Treatment*

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**Background:** Suicidal ideation (SI) is a cardinal aspect of major depressive disorder (MDD); however, patient-reported outcomes data from large-scale surveys are limited concerning SI in the context of MDD. This study aims to understand the association between varying levels of SI and health-related quality of life (HRQoL), work productivity, healthcare resource utilization (HRU), and associated costs in patients with moderately severe/severe MDD.

**Methods:** This was a retrospective, cross-sectional analysis of 2013 national survey data. Patients who self-reported moderately severe or severe MDD and completed the Short Form Survey Version 2 (SF-36v2), Work Productivity Loss and Activity Impairment questionnaire (WPAI), and questions related to HRU were analyzed. Direct and indirect costs were calculated. Patients were categorized and analyzed by the level of SI (no SI, low, moderate, and high) based on their response to Item 9 of the Patient Health Questionnaire-9.

**Results:** Among 75,000 respondents, 15.3% self-reported receiving a physician diagnosis of moderately severe or severe MDD and 2.8% of the total sample endorsed some level of SI. Patients with high SI showed a higher burden than patients with no SI, reporting lower mean SF-36v2 mental component summary scores ( $p<0.001$ ), higher work productivity loss ( $p=0.039$ ), and higher numbers of per patient per month hospitalizations ( $p=0.002$ ) and emergency room visits ( $p=0.011$ ). High SI was associated with greater per patient per month direct costs (\$1220 vs \$796;  $p=0.002$ ) and indirect costs (\$1449 vs \$1058;  $p=0.001$ ) compared with no SI. When patients with low or moderate SI were compared with patients with no SI, the results were mixed.

**Conclusion:** Higher levels of SI were associated with lower HRQoL, greater HRU, and more work impairment resulting in higher direct and indirect costs compared with patients with MDD but no SI. These results highlight the need to implement effective treatment models and interventions in the employed population.

**Keywords:** major depression, suicidal ideation, economic burden, health-related quality of life

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## Introduction

Major depressive disorder (MDD) is a common, serious mood disorder with symptoms lasting for  $\geq 2$  weeks that can vary from mild to severe and affect feelings, thoughts, and daily activities.<sup>1,2</sup> Depression is the leading cause of disability worldwide<sup>3,4</sup> and is associated with significant health-related quality of life (HRQoL) impairment and economic burden.<sup>5–8</sup> In 2018, an estimated 17.7 million adults in the United States (US) had at least 1 major depressive episode in the past year, representing approximately 7.2% of the adult population;<sup>9</sup> the lifetime prevalence rate of major depressive episodes in the US has been estimated to be as high as 20.6%.<sup>10</sup> The incremental economic burden of MDD in the US is considerable; in 2010, it was approximately \$210.5 billion.<sup>7</sup> This burden varies by the severity of depression symptoms; in a study of adults with treatment-resistant MDD, all-cause total healthcare costs, adjusted for baseline characteristics, were significantly greater for patients with moderate and severe depression symptoms relative to those with mild symptoms (\$3455 and \$5150 per patient per year, respectively).<sup>8</sup>

Suicidal ideation (SI) is a cardinal aspect of MDD.<sup>11</sup> The link between MDD and suicide has been well established,<sup>12</sup> with an estimated 31% of US adults with MDD experiencing past-year SI in 2017 (an increase from 26% in 2009).<sup>13</sup> Suicide-related costs among patients with MDD are substantial; such costs were estimated to be \$9.7 billion in the US in 2010, which was approximately 5% of the total incremental economic burden of adults with MDD.<sup>7</sup>

In the overall US population, suicide rates have been increasing,<sup>14</sup> and MDD is among the most prevalent conditions associated with SI and suicidal behavior.<sup>15</sup> While the humanistic and economic burden of MDD and SI have been investigated individually,<sup>5–8,16,17</sup> less is known about the association between SI and the burden experienced by patients with MDD. The serious nature of SI suggests that its presence could lead to reduced HRQoL and increased economic burden. However, levels of SI vary across a spectrum and detecting its presence can be difficult. Moreover, the effect of SI could be subtle, such as decreasing work productivity or increasing utilization of acute care services. Given these potential challenges, the current study employed a broad, US-based survey that collected data from the Patient Health Questionnaire-9 (PHQ-9) to provide important insights into this patient population. The

PHQ-9, a patient self-reported instrument, is aligned with the Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition symptom criteria for MDD and has been validated as a useful tool for the screening of depressive disorders and as a reliable and valid measure of depression symptom severity.<sup>18,19</sup> Additionally, it has been shown to have a high sensitivity to identify patients who are at increased risk for suicide attempt or death over a range of risk levels.<sup>20–23</sup>

In the current study, we evaluated HRQoL, work productivity, healthcare resource utilization (HRU), and economic burden for patients with a diagnosis of moderately severe or severe MDD by increasing levels of SI in an effort to better understand how SI may be associated with these parameters.

## Materials and Methods

### Data Source

This was a retrospective, cross-sectional study that used the US National Health and Wellness Survey (NHWS), a self-report survey of the US adult population. The NHWS is a large, yearly, general health survey of US adults (18+ years). The survey instrument and study procedures used in the survey were reviewed and approved by the Essex Institutional Review Board (Lebanon, NJ). All participants provided informed consent. For the current study, data from the 2013 US NHWS (N=75,000) were used.

### Sample

Adult patients who self-reported a physician diagnosis of depression and a score of  $\geq 15$  on the PHQ-9<sup>24</sup> were categorized as having moderately severe or severe MDD and were included in the analysis. PHQ-9 scores of 5, 10, 15, and 20 were previously identified as valid and responsible thresholds for the lower limits of mild, moderate, moderately severe, and severe depression, respectively, and scores of  $\geq 15$  were shown to be highly specific in predicting the presence of major depression.<sup>18</sup> Patients who screened positive on the mood disorder questionnaire (MDQ) were excluded. The MDQ is a screening tool used to evaluate potential bipolar disorder.<sup>25</sup> Both the PHQ-9 and MDQ criteria were used to ensure that the study population specifically had MDD. Furthermore, as HRU and cost burden increase with increasing MDD severity,<sup>8</sup> the population with more severe MDD is of particular interest to clinicians and researchers.

## Measures

### Levels of Suicidal Ideation

Levels of SI were assessed using Item 9 of the PHQ-9.<sup>24</sup> Increasing scores on this item have been shown to be associated with a higher risk of suicide in short- and long-term follow-up.<sup>20,22,23</sup> Patients responded to the question: “Over the past 2 weeks, how often have you been bothered by thoughts that you would be better off dead or of hurting yourself in some way?” Patients who scored 0 (not at all) were categorized as ‘no SI: depressed but without SI’; patients who scored 1 (several days), 2 (more than half the days), or 3 (nearly every day) were categorized as ‘low SI’, ‘moderate SI’, and ‘high SI’, respectively. Based on previous research,<sup>22</sup> we expected to find a stepwise increase in the associated burden as PHQ-9 Item 9 scores increase.

### Patient Demographic and Clinical Characteristics

Demographic characteristics collected from each respondent, including age, gender, race/ethnicity, marital status, education, employment status, household income, type of health insurance, and census region based on zip code, were used to characterize the patients. Further, the following clinical characteristics were also characterized: body mass index (BMI), cigarette smoking, alcohol consumption, exercise, self-reported physical and mental comorbidities associated with depression, and Charlson comorbidity index.<sup>26</sup>

### Depression-Specific Measures

Respondents meeting the criteria for the MDD module of the survey completed additional depression-specific variables, including a family history of depression, length of diagnosis, whether the individual participated in talk therapy (yes/no), current medication(s) class(es), who prescribed the medication(s), and number of months on current medication. These variables were included to explore associations with patients’ level of SI.

### Health-Related Quality of Life

Patients’ HRQoL was measured by the Short Form Survey Version 2 (SF-36v2).<sup>27</sup> The SF-36v2 is a 36-item general validated measure of HRQoL across multiple populations.<sup>28</sup> The measure was scored as two summary scores (physical [PCS] and mental [MCS] component summary scores) and as eight specific separate domain scores (see [Appendix Table 1](#) and [Appendix Table 2](#) for domain scores). These metrics were normed such that the population mean for PCS and MCS is 50. The minimal important difference (MID), or the smallest

difference that a clinician would regard as important, is 3 points for PCS and MCS and 5 points for the eight health domain scales.<sup>29</sup> The Short Form-6 Dimension (SF-6D) health utilities index was calculated using SF-36v2 items. Scores on the SF-6D range from 0 (death) to 1 (perfect health), and the general population mean score has been found to be 0.79–0.81 among a representative sample of UK respondents<sup>30</sup> and 0.76–0.80 among US respondents.<sup>31</sup> A MID of 0.041 points has been reported for the SF-6D.<sup>32</sup>

### Work Productivity Loss and Activity Impairment

Work productivity loss and activity impairment in the past week was assessed by the 6-item Work Productivity Loss and Activity Impairment questionnaire (WPAI).<sup>33</sup> The WPAI is a validated general measure widely used across several populations.<sup>34</sup> This measure assesses presenteeism (time not productive while at work), absenteeism (time absent from work), and activity impairment (% of impairment in daily activities due to health). The overall work impairment was scored based on the aggregated absenteeism and presenteeism scores. Scores on the WPAI represent the percentage of time impaired in the past 7 days. Only respondents who were employed full- or part-time responded to the presenteeism and absenteeism questions.

### Healthcare Resource Utilization

NHWS data include the number of traditional healthcare provider (HCP) visits (eg, general practitioner, internist, psychiatrist), number of hospitalizations, and number of ER visits respondents report having in the last 6 months. Using these data, mean utilization rates for patients with each level of SI were calculated for the 6-month recall period and then divided by 6 to estimate the mean per patient per month (PPPM) utilization.

### Direct and Indirect Costs

The cost for an average HCP visit, hospitalization, and ER visit were obtained from the 2013 Medical Expenditure Panel Survey (MEPS) data.<sup>35</sup> The 2013 mean values (US dollars) for each HRU type were: ER visit (\$939), hospitalization (\$13,097), and HCP visit (\$200). To calculate mean PPPM direct costs for each HRU type, for each level of SI, the mean PPPM utilization rates were multiplied by the mean cost for the corresponding type of HRU.

Indirect costs were calculated based on responses to the WPAI for each employed respondent and by using 2013 median weekly income figures obtained from the Bureau of Labor Statistics.<sup>36</sup> For each respondent, an hourly rate

was estimated by dividing the median weekly income by the number of hours in the typical work week. Next, the number of hours missed in the last week because of one's health (absenteeism) and the number of hours not productive in the last week because of health impairment while at work (presenteeism) were multiplied by the hourly rates to arrive at total lost wages for the week. These figures were then multiplied by the average number of work weeks in a year to obtain annual estimates. Finally, costs were divided by 12 to arrive at a PPPM estimate of indirect costs.

## Analysis

The overall sample was analyzed by the level of SI. Patient demographic and clinical characteristics were assessed using descriptive statistics, using frequencies and percentages for categorical variables and means and standard deviations for continuous variables. Differences between the levels of SI groups were examined across all patient demographics, clinical characteristics, and outcomes. For categorical variables, chi-square tests were used to determine significant differences while analysis of variance was used for continuous variables. The focal comparison was between patients with high SI and those with no SI.

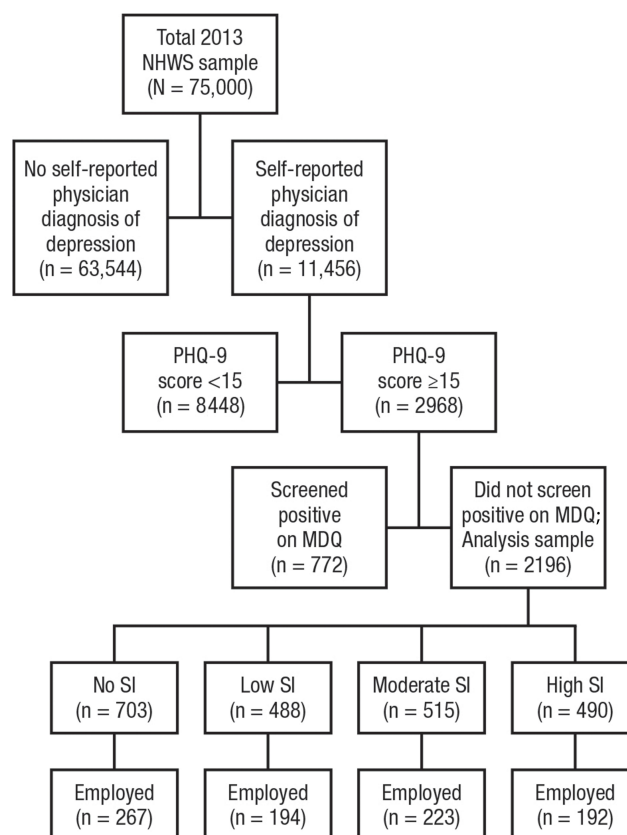
## Results

### Patient Demographics

Among 75,000 respondents to the 2013 US NHWS, 11,456 (15.3%) met the initial study inclusion criteria of a self-reported physician's diagnosis of depression. From this group of patients, the analysis sample included the 2196 patients who scored  $\geq 15$  on the PHQ-9 and screened negative on the MDQ (Figure 1). Among all patients with moderately severe or severe MDD, 68.0% reported any SI. Those reporting any level of SI were younger ( $p$ -values  $\leq 0.05$  for each SI severity group compared with the no SI group), and the proportion of males increased with increasing levels of SI ( $p$ 's  $\leq 0.01$  for each SI severity group compared with the no SI group; Table 1). Across SI groups, commercial insurance coverage was reported by 41% to 47% of patients; the high SI group had the largest proportion of uninsured patients (28%) compared with the other SI groups (Table 1).

### Clinical Characteristics

Clinical characteristics, including BMI, smoking status, and number and types of comorbidities, were generally similar across groups (Table 2). A higher proportion of patients with moderate SI (30%) and high SI (29%)



**Figure 1** Analysis sample definition.

**Notes:** Only employed patients are included in the calculation of the WPAI and indirect costs variables. HRU and direct cost outcomes include the full analysis sample. **Abbreviations:** NHWS, National Health and Wellness Survey; PHQ-9, Patient Health Questionnaire-9; MDQ, mood disorder questionnaire; SI, suicidal ideation; WPAI, Work Productivity Loss and Activity Impairment questionnaire; HRU, healthcare resource utilization.

reported social anxiety as a mental health comorbidity compared with patients with no SI (22%;  $p$ 's  $\leq 0.014$ ; Table 2). The most commonly used medications across patient groups were selective serotonin reuptake inhibitors and/or serotonin-norepinephrine reuptake inhibitors (Appendix Figure 1a and 1b). Use of bupropion, antipsychotics, and other medications was generally similar across SI groups; a higher proportion of patients with high SI (14%) and patients with moderate SI (12%) compared with those with no SI (6%) reported taking antipsychotics ( $p$ 's  $\leq 0.005$ ; Table 2).

### Health-Related Quality of Life

Patients with high SI reported significantly lower mean SF-36v2 MCS scores compared with those with no SI (25.90 [SD=10.76] vs 29.01 [SD=9.25];  $p < 0.001$ ; Table 3). Patients with high SI did not differ on their mean SF-36v2 PCS scores compared with those with no

**Table 1** Demographic Characteristics by Level of Suicidal Ideation

	A – No SI			B – Low SI			C – Moderate SI			D – High SI			P <sub>overall</sub>
	(n = 703)			(n = 488)			(n = 515)			(n = 490)			
	%	n		%	n		%	n		%	n		
Age (Years) (M, SD)	45.87	14.56		44.09*	14.48		43.08*	14.03		44.11*	14.17		0.007
Age (Years)													0.023
<21	1.85% <sub>ab,d</sub>	13		3.07% <sub>a,c,d</sub>	15		4.66% <sub>b,d</sub>	24		3.47% <sub>ab,b,c</sub>	17		
21–30	18.49% <sub>ab,c,d</sub>	130		19.47% <sub>a,c,d</sub>	95		18.83% <sub>ab,b,d</sub>	97		17.35% <sub>ab,b,c</sub>	85		
31–50	40.40% <sub>ab,c</sub>	284		41.60% <sub>a,c,d</sub>	203		46.02% <sub>ab,b,d</sub>	237		46.33% <sub>ab,c</sub>	227		
51+	39.26% <sub>b</sub>	276		35.86% <sub>a,c,d</sub>	175		30.49% <sub>b,d</sub>	157		32.86% <sub>b,c</sub>	161		
Gender (% Male)	30.58%	215		37.70% <sub>c,d</sub>	184		46.41% <sub>d</sub>	239		51.84% <sub>c</sub>	254		<0.001
Race/Ethnicity													0.259
Non-Hispanic White	74.96% <sub>ab,d</sub>	527		75.82% <sub>a,d</sub>	370		68.93% <sub>d</sub>	355		71.84% <sub>c</sub>	352		
Non-Hispanic Black	7.82% <sub>b,c,d</sub>	55		7.58% <sub>a,c,d</sub>	37		10.49% <sub>a,b,d</sub>	54		10.00% <sub>a,b,c</sub>	49		
Hispanic	9.82% <sub>b,c,d</sub>	69		9.02% <sub>a,c,d</sub>	44		12.04% <sub>a,b,d</sub>	62		8.78% <sub>a,b,c</sub>	43		
Other Ethnicity	7.40% <sub>b,c,d</sub>	52		7.58% <sub>a,c,d</sub>	37		8.54% <sub>a,b,d</sub>	44		9.39% <sub>a,b,c</sub>	46		
Marital Status (%Married/Living with Partner)	47.51% <sub>b,c,d</sub>	334		50.20% <sub>a,d</sub>	245		43.88% <sub>a,d</sub>	226		44.49% <sub>a,b,c</sub>	218		0.159
Education (% College Degree)	39.54% <sub>b,c,d</sub>	278		43.85% <sub>a,c,d</sub>	214		40.97% <sub>a,b,d</sub>	211		44.69% <sub>a,b,c</sub>	219		0.250
Employment Status													0.291
Not Employed	30.44% <sub>b,c,d</sub>	214		32.99% <sub>a,c,d</sub>	161		31.65% <sub>a,b,d</sub>	163		30.61% <sub>a,b,c</sub>	150		
Retired	14.94% <sub>d</sub>	105		10.86% <sub>c,d</sub>	53		9.32% <sub>b,d</sub>	48		12.45% <sub>a,b,c</sub>	61		
Short Term Disability	1.28% <sub>b,c,d</sub>	9		1.02% <sub>a,c,d</sub>	5		0.78% <sub>a,b,d</sub>	4		1.84% <sub>a,b,c</sub>	9		
Long Term Disability	15.36% <sub>b,c,d</sub>	108		15.37% <sub>a,c,d</sub>	75		14.95% <sub>a,b,d</sub>	77		15.92% <sub>a,b,c</sub>	78		
Employed	37.98% <sub>b,c,d</sub>	267		39.75% <sub>a,c,d</sub>	194		43.30% <sub>a,b,d</sub>	223		39.18% <sub>a,b,c</sub>	192		
Household Income													0.299
<\$25k	34.00% <sub>b,c,d</sub>	239		29.10% <sub>a,d</sub>	142		37.09% <sub>a,d</sub>	191		33.88% <sub>a,b,c</sub>	166		
\$25k to \$50k	31.72% <sub>b,c,d</sub>	223		31.76% <sub>a,c,d</sub>	155		29.51% <sub>a,b,d</sub>	152		31.63% <sub>a,b,c</sub>	155		
\$50k to \$75k	16.64% <sub>b,c,d</sub>	117		17.21% <sub>a,c,d</sub>	84		13.20% <sub>a,b,d</sub>	68		13.88% <sub>a,b,c</sub>	68		
\$75k or More	13.66% <sub>b,c,d</sub>	96		17.42% <sub>a,c,d</sub>	85		16.31% <sub>a,b,d</sub>	84		15.31% <sub>a,b,c</sub>	75		
Decline to Answer	3.98% <sub>b,c,d</sub>	28		4.51% <sub>a,c,d</sub>	22		3.88% <sub>a,b,d</sub>	20		5.31% <sub>a,b,c</sub>	26		
Insurance													0.103
Commercial	42.25% <sub>b,c,d</sub>	297		46.52% <sub>d</sub>	227		40.97% <sub>a,d</sub>	211		40.61% <sub>a,b,c</sub>	199		0.005
Medicaid	14.79% <sub>c,d</sub>	104		8.81% <sub>a,d</sub>	43		15.92% <sub>a,d</sub>	82		13.06% <sub>a,c</sub>	64		

(Continued)

Table 1 (Continued).

	A – No SI (n = 703)			B – Low SI (n = 488)			C – Moderate SI (n = 515)			D – High SI (n = 490)		
Medicare Other No Insurance	25.18% <sub>b,c,d</sub> 6.69% <sub>b,c,d</sub> 22.33% <sub>b,c</sub>	177 47 157		21.52% <sub>a,c,d</sub> 6.56% <sub>a,c,d</sub> 24.80% <sub>a,c,d</sub>	105 32 121		21.36% <sub>a,b,d</sub> 4.27% <sub>a,b,d</sub> 24.27% <sub>a,b,d</sub>	110 22 125		22.04% <sub>a,b,c</sub> 3.88% <sub>a,b,c</sub> 28.37% <sub>b,c</sub>	108 19 139	0.475 0.115 0.126
BMI (kg/m <sup>2</sup> ) Underweight (<18.5) Normal (18.5–25) Overweight (25–30) Obese (>30) Decline to Answer	2.56% <sub>b,c,d</sub> 21.91% <sub>b,c,d</sub> 24.61% <sub>b,c,d</sub> 49.08% <sub>b,d</sub> 1.85% <sub>b,c,d</sub>	18 154 173 345 13		2.46% <sub>a,c,d</sub> 25.82% <sub>a,c,d</sub> 25.41% <sub>a,c,d</sub> 44.26% <sub>a,c,d</sub> 2.05% <sub>a,c,d</sub>	12 126 124 216 10		2.91% <sub>a,b,d</sub> 22.72% <sub>a,b,d</sub> 29.13% <sub>a,b,d</sub> 42.14% <sub>b,d</sub> 3.11% <sub>a,b,d</sub>	15 117 150 217 16		2.65% <sub>a,b,c</sub> 26.12% <sub>a,b,c</sub> 24.49% <sub>a,b,c</sub> 43.88% <sub>a,b,c</sub> 2.86% <sub>a,b,c</sub>	13 128 120 215 14	0.390
Smoking Status Current Smoker Former Smoker Never Smoker	28.59% <sub>b,c,d</sub> 30.01% <sub>b,c,d</sub> 41.39% <sub>b,c,d</sub>	201 211 291		30.74% <sub>a,c,d</sub> 27.87% <sub>a,c,d</sub> 41.39% <sub>a,c,d</sub>	150 136 202		30.87% <sub>a,b,d</sub> 28.54% <sub>a,b,d</sub> 40.58% <sub>a,b,d</sub>	159 147 209		29.18% <sub>a,b,c</sub> 25.51% <sub>a,b,c</sub> 45.31% <sub>a,b,c</sub>	143 125 222	0.611
Currently Drink	60.74% <sub>b,c,d</sub>	427		61.27% <sub>a,c,d</sub>	299		63.88% <sub>a,b,d</sub>	329		58.78% <sub>a,b,c</sub>	288	0.418
Currently Exercise	49.93% <sub>b,d</sub>	351		48.77% <sub>a,d</sub>	238		59.61%	307		52.65% <sub>a,b</sub>	258	0.002
Comorbidity Index (M, SD)	0.60	1.13		0.70	1.35		0.63	1.43		0.74	1.63	0.290
Census Region North East Midwest South West	15.22% <sub>b,d</sub> 27.03% <sub>b,c,d</sub> 35.70% <sub>b,c,d</sub> 22.05% <sub>b,c,d</sub>	107 190 251 155		16.60% <sub>a,c,d</sub> 26.23% <sub>a,c,d</sub> 34.84% <sub>a,c,d</sub> 22.34% <sub>a,c,d</sub>	81 128 170 109		21.17% <sub>b,d</sub> 25.63% <sub>a,b,d</sub> 32.23% <sub>a,b,d</sub> 20.97% <sub>a,b,d</sub>	109 132 166 108		18.16% <sub>a,b,c</sub> 25.31% <sub>a,b,c</sub> 35.31% <sub>a,b,c</sub> 21.22% <sub>a,b,c</sub>	89 124 173 104	0.513

**Notes:** \* $p < 0.05$  compared to "No SI". For pairwise comparisons, refer to subscripts (eg a, b, c, d) attached to means or cell counts in the same row that do not share the same subscript (eg XX<sub>a</sub> vs XX<sub>b</sub>) are significantly different at  $p < 0.05$ . If they share the same subscript (eg XX<sub>a</sub> vs XX<sub>a</sub> or XX<sub>a,b</sub> vs XX<sub>a</sub>) then they are not significantly different at  $p < 0.05$ .

**Abbreviations:** SI, suicidal ideation; M, mean; SD, standard deviation; BMI, body mass index.



**Table 2** Comorbidities and Depression-Specific Variables by Level of Suicidal Ideation Among Patients with Moderately Severe or Severe MDD

	A – No SI (n = 703)			B – Low SI (n = 488)			C – Moderate SI (n = 515)			D – High SI (n = 490)			p <sub>overall</sub>	p <sub>A vs B</sub>	p <sub>A vs C</sub>	p <sub>A vs D</sub>
	(n = 703)			(n = 488)			(n = 515)			(n = 490)						
	%	n	%	n	%	n	%	n	%	n						
Physical																
Hypertension	42.82%	301	33.81%	165	40.78%	210	35.10%	172	0.004	0.002	0.476	0.007				
Anemia	10.38%	73	8.40%	41	7.57%	39	8.98%	44	0.370	0.253	0.093	0.422				
Rheumatoid Arthritis	3.27%	23	4.51%	22	3.88%	20	4.08%	20	0.736	0.271	0.568	0.460				
HIV or AIDS	0.28%	2	0.41%	2	0.39%	2	0.41%	2	0.980	0.713	0.754	0.716				
Hepatitis A	0.71%	5	0.82%	4	0.97%	5	0.61%	3	0.924	0.832	0.620	0.837				
Hepatitis B	0.14%	1	1.23%	6	1.36%	7	0.61%	3	0.059	0.016	0.009	0.167				
Hepatitis C	2.70%	19	1.23%	6	1.55%	8	1.22%	6	0.151	0.081	0.178	0.079				
Chronic Kidney Disease	1.56%	11	2.66%	13	1.75%	9	1.43%	7	0.451	0.184	0.804	0.849				
Chronic Heart Failure	3.41%	24	3.07%	15	2.72%	14	3.47%	17	0.889	0.746	0.490	0.959				
Diabetes Type 1 or Type 2	18.78%	132	15.16%	74	17.28%	89	17.55%	86	0.451	0.105	0.504	0.590				
Arrhythmia	4.69%	33	4.71%	23	3.11%	16	3.88%	19	0.491	0.988	0.164	0.497				
Mental																
Anxiety	65.43%	460	64.34%	314	60.19%	310	59.59%	292	0.102	0.698	0.061	0.040				
Social Anxiety	22.33%	157	25.41%	124	29.90%	154	28.57%	140	0.014	0.219	0.003	0.014				
Panic Disorder	18.78%	132	19.47%	95	23.50%	121	17.55%	86	0.090	0.765	0.045	0.590				
Sleep Disorder	51.92%	365	47.75%	233	41.17%	212	45.71%	224	0.003	0.156	0.000	0.035				
ADD/ADHD	8.53%	60	5.33%	26	5.05%	26	8.16%	40	0.033	0.035	0.019	0.820				
Alcoholism	4.69%	33	7.99%	39	7.77%	40	5.31%	26	0.043	0.019	0.026	0.632				
Suicide Ideation	0.00%	0	100.00%	488	100.00%	515	100.00%	490	<0.001	<0.001	<0.001	<0.001				
Family History of Depression (% Yes)	52.8%	371	51.4%	251	52.2%	269	52.7%	258	0.972	0.649	0.852	0.967				
Length of Diagnosis (Years; mean, SD)	3.37	0.94	3.40	0.91	3.35	0.92	3.36	0.95	0.884	0.559	0.812	0.958				
Participates in Talk Therapy (% Yes) <sup>a</sup>	21.3%	150	24.8%	121	25.0%	129	26.7%	131	0.161	0.162	0.128	0.031				
Who Prescribed Your Medication?									0.854	0.946	0.745	0.342				
PCP	38.4%	270	35.5%	173	33.4%	172	32.2%	158								
NP/PA	4.6%	32	4.7%	23	4.3%	22	3.3%	16								
Psychiatrist	20.2%	142	19.1%	93	21.0%	108	21.8%	107								
Other	2.0%	14	2.3%	11	1.9%	10	2.2%	11								
Medication Class (% Currently Using)																
SSRI/SNRI	54.6%	384	49.8%	243	50.1%	258	46.3%	227	0.190	0.311	0.674	0.036				
Bupropion	11.2%	79	11.3%	55	9.1%	47	10.4%	51	0.737	0.702	0.421	0.939				

(Continued)

Table 2 (Continued).

	A – No SI (n = 703)		B – Low SI (n = 488)		C – Moderate SI (n = 515)		D – High SI (n = 490)						
Other Antidepressants	9.0%	63	10.7%	52	9.1%	47	10.4%	49	0.523	0.179	0.610	0.257	
Antipsychotics	3.8%	27	4.7%	23	7.0%	36	8.2%	40	0.001	0.337	0.005	<0.001	
Other- Unspecified	3.3%	23	2.7%	13	3.9%	20	4.5%	22	0.439	0.547	0.568	0.277	
Months on Medication									0.451	0.273	0.711	0.686	
1–2 Months	6.5%	46	6.1%	30	6.0%	31	4.9%	24					
3–5 Months	4.3%	30	4.9%	24	3.3%	17	4.9%	24					
6–8 Months	6.4%	45	3.9%	19	5.2%	27	4.7%	23					
9–11 Months	1.3%	9	2.3%	11	0.6%	3	1.0%	5					
12 + Months	46.7%	328	44.3%	216	45.4%	234	44.1%	216					

Note: \*This question was asked of all people who reported experiencing depression in the past 12 months, regardless of whether they also reported a diagnosis.

Abbreviations: SI, suicidal ideation; MDD, major depressive disorder; HIV, human immunodeficiency virus; AIDS, acquired immunodeficiency syndrome; ADD, attention-deficit disorder; ADHD, attention-deficit/hyperactivity disorder; SD, standard deviation; PCP, primary care provider; NP, nurse practitioner; PA, physician assistant; SSRI, selective serotonin reuptake inhibitor; SNRI, serotonin-norepinephrine reuptake inhibitor.

SI ( $p=0.796$ ). Patients with high SI also reported significantly lower mean SF-6D health utility index scores compared with those with no SI (0.52 [SD=0.11] vs 0.54 [SD=0.09];  $p < 0.001$ ; Table 3).

## Work Productivity and Activity Impairment and Indirect Costs

Among employed patients, work productivity was not statistically significant across all levels of SI ( $p=0.104$ ); however, patients with high SI showed significantly higher work productivity loss (absenteeism and presenteeism combined; 45% vs 39%;  $p=0.039$ ; Table 3) compared with those with no SI. For example, this would equate to 18 hours of work productivity impairment per person compared with 15.6 impaired hours for an average 40-hour work week. Patients with high SI had higher activity impairment (60% vs 57%;  $p=0.087$ ; Table 3) compared with those with no SI; however, this difference did not reach statistical significance. Patients with high SI incurred greater PPPM indirect costs (\$1449 vs \$1058;  $p=0.001$ ; Table 3) compared with patients with no SI.

## Healthcare Resource Utilization and Direct Costs

Patients with high SI reported significantly higher monthly rates of hospitalizations and ER visits compared with those with no SI ( $p$ 's  $< 0.002$ ; Table 3 and Figure 2), although there was no difference in HCP visits between these groups ( $p=0.679$ ). Patients with high SI incurred greater PPPM direct costs (\$1220 vs \$796;  $p=0.002$ ; Table 3) compared with those with no SI. Considering the total PPPM direct and indirect costs, monthly total costs for patients with high SI (\$2475) were significantly higher than for those with no SI (\$1714;  $p=0.010$ ).

## Discussion

To gain insights into the humanistic and economic burden of varying levels of SI in the context of MDD, we analyzed patients with moderately severe or severe MDD experiencing SI using the NHWS. Patients endorsing Item 9 of the PHQ-9, who comprised 2.0% of all NHWS respondents, were younger, more often male, and more often uninsured.

Health utilities observed in patients with high SI were significantly lower than in patients without SI. These utilities represent levels of overall HRQoL as low or lower than those observed in certain cancers and chronic pain.<sup>37,38</sup> Patients with

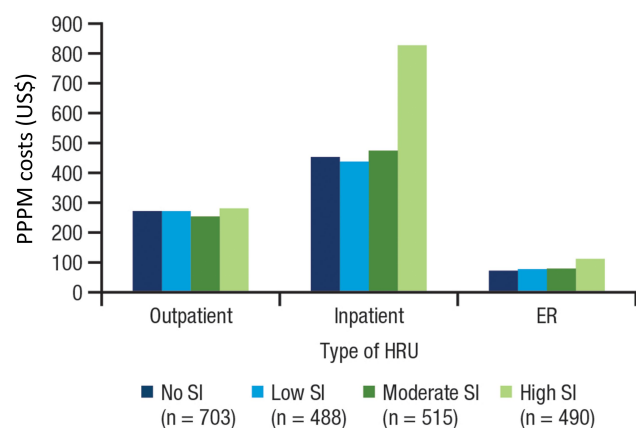


**Table 3** Health Outcomes and Direct and Indirect Costs by Level of Suicidal Ideation Among Patients with Moderately Severe or Severe MDD

	A – No SI		B – Low SI		C – Moderate SI		D – High SI						
	(n = 703)		(n = 488)		(n = 515)		(n = 490)						
	M	SD	M	SD	M	SD	M	SD	p <sub>overall</sub>				
Health Status (SF-36v2)													
Mental Component Summary	29.01	9.25	28.18	8.50	29.04	9.36	25.90	10.76	<0.001	0.140	0.946	<0.001	
Physical Component Summary	44.60	12.15	44.25	12.13	46.12	11.60	44.42	12.70	0.051	0.624	0.031	0.796	
Health Utilities (SF-6D)	0.54	0.09	0.53	0.08	0.55	0.09	0.52	0.11	<0.001	0.100	0.285	<0.001	
Work Productivity (WPAI) <sup>a</sup>	(n = 267)		(n = 194)		(n = 223)		(n = 192)						
Absenteeism	8.86	21.17	11.17	24.39	12.07	24.19	11.07	20.69	0.462	0.290	0.129	0.312	
Presenteeism	34.88	28.99	40.28	29.16	39.27	28.66	41.21	31.76	0.112	0.063	0.116	0.029	
Work Productivity Loss	38.88	31.95	45.20	31.71	43.96	31.83	45.32	33.43	0.104	0.042	0.091	0.039	
Activity Impairment	56.51	29.10	58.30	27.80	53.59	29.58	59.51	32.54	0.010	0.309	0.090	0.087	
Resource Use (per Patient per Month)													
No. of PCP Visits	1.36	1.76	1.36	1.65	1.27	1.79	1.40	2.10	0.681	0.987	0.385	0.679	
No. of Hospitalizations	0.03	0.14	0.03	0.18	0.04	0.10	0.06	0.19	0.004	0.899	0.854	0.002	
No. of ER Visits	0.08	0.20	0.08	0.20	0.08	0.19	0.12	0.30	0.009	0.650	0.547	0.001	
PHQ-9 Total Score	17.57	2.44	18.01	2.78	18.71	2.53	22.97	3.79	<0.001	0.010	0.000	<0.001	
Indirect Costs (US\$, per Patient per Month) <sup>a</sup>													
Absenteeism	246.90	651.51	325.45	787.36	336.22	745.01	366.46	840.54	0.368	0.278	0.203	0.100	
Presenteeism	862.69	859.08	981.46	928.82	978.35	948.51	1135.37	1166.91	0.042	0.215	0.210	0.004	
Total	1057.70	1086.49	1182.46	1090.91	1247.83	1246.29	1448.55	1471.70	0.012	0.300	0.102	0.001	
Direct Costs (US\$, per Patient per Month)													
HCP Visits	271.79	351.59	271.45	330.34	253.40	358.02	280.68	419.53	0.681	0.987	0.385	0.679	
ER Visits	71.68	185.52	77.29	183.56	79.01	179.04	111.47	283.30	0.009	0.650	0.547	0.011	
Hospitalizations	452.71	1786.81	437.75	2300.31	474.06	1302.95	827.45	2523.60	0.004	0.899	0.854	0.002	
Total	796.18	2045.80	786.49	2520.73	806.47	1567.77	1219.59	2911.21	0.005	0.943	0.938	0.002	
Total Costs (US\$, per Patient per Month)													
Indirect and Direct	1714.18	2497.74	2061.91	4020.53	1992.72	2130.81	2474.61	3267.58	0.080	0.239	0.328	0.010	

**Notes:** Both indirect and direct costs reflect monthly values. <sup>a</sup>Only employed patients are included in the calculation of the WPAI and indirect costs variables. SF-36v2 uses a recall period of 4 weeks; WPAI uses a recall period of 7 days; PHQ-9 uses a recall period of 2 weeks; resource use was originally reported for the previous 6 months.

**Abbreviations:** SI, suicidal ideation; MDD, major depressive disorder; M, mean; SD, standard deviation; SF-36v2, Short Form Survey Version 2; SF-6D, Short Form-6 Dimension; WPAI, Work Productivity Loss and Activity Impairment questionnaire; PCP, primary care provider; ER, emergency room; PHQ-9, Patient Health Questionnaire-9; US\$, United States Dollars; HCP, healthcare provider.



**Figure 2** Direct per patient per month costs by level of suicidal ideation and type of healthcare resource utilization among patients with moderately severe or severe MDD. **Abbreviations:** PPPM, per patient per month; US\$, United States dollars; SI, suicidal ideation; ER, emergency room; HRU, healthcare resource utilization.

high SI had higher work productivity loss resulting in higher indirect costs compared with patients with no SI, which is unsurprising in the context of such low HRQoL. The results of this study showed most of the indirect cost was due to impairment at work (ie, presenteeism), suggesting that patients often show up to work despite the severity of their condition and demonstrate low productivity. The association between presenteeism and SI among patients with MDD is consistent with observations in a European population.<sup>39</sup> Moreover, results from a previous study evaluating the relationship between depression symptoms and presenteeism have shown that cognitive symptoms accompanying depression, such as impaired concentration, anhedonia, and self-criticism, had a significant impact on presenteeism but were less important in predicting absenteeism.<sup>40</sup> Using a multivariate model to compare patterns and severity of self-reported productivity impairment across several different medical conditions, depression was associated with the highest odds of problems with mental/interpersonal functioning tasks and with overall output.<sup>41</sup> A linear relationship has been demonstrated in the literature, with more severe depression symptoms correlated with increased presenteeism.<sup>40,42</sup> Poor work adjustment may be an important risk factor for suicidal behavior in people with mood disorders.<sup>43</sup> One study showed that while overall social adjustment was not associated with suicide attempt history, individuals with poor work adjustment were significantly more likely to report a history of a suicide attempt.<sup>44</sup>

Among the patients with moderately severe or severe MDD in the current study, those with high SI had significantly higher rates of hospitalization and ER visits than those with no SI. While not all patients experience hospitalization or seek

care, the cost of hospitalization accounted for the largest portion of direct costs in this study. These results support previous studies showing the high impact of hospitalization on the economic burden associated with MDD and SI.<sup>7,45</sup> In 2010, almost \$100 billion of the estimated \$210.5 billion economic burden of MDD in the US was attributable to direct medical costs, and \$20.5 billion was due to inpatient medical services.<sup>7</sup> Data from the Agency for Healthcare Research and Quality reported that, in 2013, over 70% of emergency department (ED) visits related to SI resulted in admission or transfer to another hospital or facility compared with only 19% of all other ED visits.<sup>46</sup> Among these SI-related ED visits that resulted in admissions, the aggregate cost of ED and inpatient care increased by 20% annually from 2006 to 2013.<sup>46</sup>

Such high HRQoL and economic burden highlight the need for effective screening and management of patients with MDD and SI. Considering the risk to these patients, it is important to note that several validated screening instruments to detect depression have been utilized in the primary care setting,<sup>47</sup> however, challenges remain in identifying those at risk of suicidality.<sup>48,49</sup> The PHQ-9 is a practical way to screen for and assess depression symptom severity in the real world given its inclusion in National Quality Forum (NQF)-endorsed quality measures, inclusion in Healthcare Effectiveness Data and Information Set (HEDIS) and Merit-based Incentive Payment System (MIPS) measures, and ease and frequency of use.<sup>24</sup>

Multiple health systems have published guidelines referencing or endorsing the use of the PHQ-9 in the screening and management of depression. One example is Kaiser Permanente which published a guideline specifically including recommendations around screening and treatment based on the PHQ-9.<sup>50</sup> The Department of Defense and Department of Veterans Affairs published joint guidelines recommending the use of the PHQ-9 for initial measurement of depression severity as well as treatment monitoring.<sup>51</sup> These examples support the use of the PHQ-9 in depression screening, making this tool even more relevant to clinicians. With routine use, there is an opportunity to more effectively identify patients with MDD, and to better identify patients with SI, providing a chance for treatment and management of these at-risk individuals.

## Limitations

Despite the insight that this study provides into the burden associated with SI in patients with moderately severe or severe MDD, several limitations should be considered. First, the data source used for this analysis was based on a cross-sectional

study design that does not permit causal conclusions to be drawn. The data were collected from self-reports of patients responding to a survey conducted online, and thus responses may be subject to recall bias, could not be objectively confirmed through review of medical records (including diagnosis of MDD), and may overrepresent certain types of individuals who are more comfortable with online engagement. Of note, the instruments used in the data source did possess relatively short recall periods and thus should have limited the degree to which recall bias influenced study results. However, because the work productivity measure reports only the prior week's functioning, we are unable to establish conclusions regarding long-term impact or association. Moreover, different outcome measures had varying recall periods (ie, 4 weeks for SF-36v2, 7 days for WPAI, 6 months for HRU, and 2 weeks for the PHQ-9). Nevertheless, the results reported here trended as expected and were consistent with similar studies.<sup>6,7,16,39,45,46</sup>

The second limitation of this study was the absence of a clinical measure to categorize patients based on their level of SI. This analysis relied on using Item 9 on the PHQ-9 to form the basis for assessing patients' suicidal level in the analysis, as it has been associated with the risk of suicide.<sup>20,22,23</sup> However, limitations may exist in the wording of this question. The PHQ-9 asks about the presence of either thoughts of being dead, without specifically asking about suicide ("you would be better off dead"), or thoughts of self-injury ("hurting yourself in some way"). Moreover, the range of responses, including "several days" and "more than half of the days", may be confusing for respondents, particularly if they did not consider the appropriate recall period of 2 weeks.

Additional limitations include the non-random assignment of patients based on their level of SI, which could lead to imbalances in risk factors between subpopulations and thus bias results. Since patients included in the analysis self-reported their physician diagnosed depression, the data do not provide codes to allow examination of specific depression subtypes. All combined, these limitations may limit the comparability and generalizability of the results.

## Conclusions

Higher levels of SI among patients with moderately severe or severe MDD were associated with significantly lower HRQoL, greater HRU, and greater work impairment resulting in higher direct and indirect costs compared with patients reporting no SI. These findings emphasize the importance of examining

direct, indirect, and total costs for patients with MDD experiencing SI. Considering the increased HRQoL and economic burden among patients with moderately severe or severe MDD and high SI observed in this study, from the payer and employer perspectives, it is important to ensure these patients are identified and receive appropriate intervention to avoid further worsening of their SI levels and increased economic burden.

## Abbreviations

BMI, body mass index; ED, emergency department; ER, emergency room; HCP, healthcare provider; HEDIS, Healthcare Effectiveness Data and Information Set; HRQoL, health-related quality of life; HRU, healthcare resource utilization; MCS, mental component summary; MDD, major depressive disorder; MDQ, mood disorder questionnaire; MEPS, Medical Expenditure Panel Survey; MID, minimal important difference; MIPS, Merit-based Incentive Payment System; NHWS, National Health and Wellness Survey; NQF, National Quality Forum; PCS, physical component summary; PHQ-9, Patient Health Questionnaire-9; PPPM, per patient per month; SD, standard deviation; SF-6D, Short Form-6 Dimension; SF-36v2, Short Form Survey Version 2; SI, suicidal ideation; UK, United Kingdom; US, United States; WPAI, Work Productivity Loss and Activity Impairment questionnaire.

## Data Sharing Statement

The data that support the findings of this study are available from Kantar Health but restrictions apply to the availability of these data, which were used under license for the current study, and so are not publicly available. Data are however available from Carmela Benson (CBenson5@its.jnj.com) upon reasonable request and with permission of Kantar Health.

## Acknowledgments

The authors acknowledge Errol J. Philip, PhD for his assistance with literature review and writing. Editorial support was provided by Courtney St. Amour, PhD, of MedErgy, and funded by Janssen Scientific Affairs, LLC. David Singer is currently affiliated with Boehringer Ingelheim Pharmaceuticals, Inc.; Colleen M. Carpinella is currently affiliated with Thermo Fisher Scientific; May Shawi is currently affiliated with Janssen Research & Development, LLC; and Larry Alphas is currently a consultant at Larry Alphas, MD, PhD Consulting.

## Author Contributions

All authors made substantial contributions to conception and design, acquisition of data, or analysis and interpretation of data; took part in drafting the article or revising it critically for important intellectual content; agreed to submit to the current journal; gave final approval of the version to be published; and agree to be accountable for all aspects of the work.

## Funding

This study was funded by Janssen Scientific Affairs, LLC.

## Disclosure

Carmela Benson is a full-time employee of Janssen Scientific Affairs, LLC. May Shawi and Larry Alphs were full-time employees of Janssen Scientific Affairs, LLC at the time of the study. David Singer was a post-doctoral fellow with Thomas Jefferson University and reports a grant from Janssen Scientific Affairs, LLC at the time of the study. Colleen M. Carpinella was an employee of Kantar Health, which conducted this study with funding from Janssen Scientific Affairs, LLC, at the time of the study. The authors report no other conflicts of interest in this work.

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