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The Economic Burden of Adults With Major Depressive Disorder in the United States (2005 and 2010)

Paul E. Greenberg, MS, MA; Andree-Anne Fournier, MA; Tammy Sisitsky, MA; Crystal T. Pike, MBA; and Ronald C. Kessler, PhD

ABSTRACT

Background: The economic burden of depression in the United States—including major depressive disorder (MDD), bipolar disorder, and dysthymia—was estimated at $83.1 billion in 2000. We update these findings using recent data, focusing on MDD alone and accounting for comorbid physical and psychiatric disorders.

Method: Using national survey (*DSM-IV* criteria) and administrative claims data (*ICD-9* codes), we estimate the incremental economic burden of individuals with MDD as well as the share of these costs attributable to MDD, with attention to any changes that occurred between 2005 and 2010.

Results: The incremental economic burden of individuals with MDD increased by 21.5% (from $173.2 billion to $210.5 billion, inflation-adjusted dollars). The composition of these costs remained stable, with approximately 45% attributable to direct costs, 5% to suicide-related costs, and 50% to workplace costs. Only 38% of the total costs were due to MDD itself as opposed to comorbid conditions.

Conclusions: Comorbid conditions account for the largest portion of the growing economic burden of MDD. Future research should analyze further these comorbidities as well as the relative importance of factors contributing to that growing burden. These include population growth, increase in MDD prevalence, increase in treatment cost per individual with MDD, changes in employment and treatment rates, as well as changes in the composition and quality of MDD treatment services.

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Corresponding author: *Paul E. Greenberg, MS, MA, Analysis Group, Inc, 111 Huntington Ave, 10th Floor, Boston, MA 02199 (paul.greenberg@analysisgroup.com).*

Depression is among the most burdensome disorders worldwide, giving rise to considerable adverse effects on activities of daily living for extended periods of time.[1,2] In the United States, it is a leading cause of disability for people aged 15–44 years, resulting in almost 400 million disability days per year, substantially more than most other physical and mental conditions.[3,4] The economic burden of depression, including major depressive disorder (MDD), bipolar disorder, and dysthymia, was estimated at $83.1 billion in 2000 in the United States.[5] This total was composed of $26.1 billion in direct medical costs, $5.4 billion in suicide-related mortality costs, and $51.5 billion in indirect workplace costs (absenteeism from work and presenteeism while at work).[5] Several subsequent studies have quantified specific components of the cost of depression, such as workplace costs or outpatient treatment costs.[6–8] Other studies have analyzed the economic burden of closely related conditions, such as treatment-resistant depression.[9] However, no study has attempted to quantify the overall economic burden of MDD. In addition, although recent literature highlights the importance of comorbidities among people with depression,[10,11] prior estimates focused on the cost of depression alone, with no attention to the added economic burden from physical and psychiatric comorbidities.[5,12]

The objectives of the current study are to examine (1) excess costs incurred by adults with compared to those without MDD having otherwise similar profiles, (2) the portion of these costs attributable to MDD itself as opposed to comorbid conditions, and (3) the relative importance of the different components of the overall economic burden of MDD, with attention to direct costs, suicide-related costs, and workplace costs. In doing so, we update previous research with attention to any changes that occurred between 2005 and 2010. In the absence of a single database from which to draw, we rely on findings from the literature to supplement original results.

METHOD

Key elements of the method are described below. Our framework for evaluating the economic burden of adults with MDD is also summarized in Supplementary eTable 1.

Prevalence Data

Prevalence rates by gender, age, employment, and treatment status relied on the 2005 and 2010 updates to the National Survey on Drug Use and Health (NSDUH), a national probability sample of the adult US civilian, noninstitutionalized population.[13,14] In the NSDUH depression module, adult respondents were asked questions adapted from the National Comorbidity Survey Replication,[15,16] which was based on World Health Organization World Mental Health Survey Initiative version of the Composite International Diagnostic Interview. On the basis of these responses, *DSM-IV* criteria[17] were used to identify people with a past-year major depressive episode (MDE), defined as symptoms occurring for a period of 2 weeks or longer over the past 12 months among those with lifetime MDE.[18]

Cost Data: Sample and Control Group

Individuals aged 18–64 years with diagnosed MDD in 2005 or 2010 (study years) were selected from the OptumHealth Reporting and Insights administrative

Clinical Points

- The cost of major depressive disorder in the United States is known to be substantial, but little attention has been given to the added economic burden from physical and psychiatric comorbidities.
- Comorbid conditions account for the largest portion of the growing economic burden of major depressive disorder and should be considered in the treatment of the disease.

claims database.[19,20] This private insurance database includes over 16 million beneficiaries (ie, employees, spouses, and dependents) from 69 large, self-insured US companies. Patients with MDD were included for analysis if they had at least 2 *ICD-9-CM* claims for MDD—296.2 (single episode) or 296.3 (recurrent episode)—occurring on different dates during 1 of the 2 study years. To ensure that a complete claims history was available, each patient was required to have continuous health care eligibility during the study period. Patients with MDD having health maintenance organization, capitated, or Medicare coverage were excluded from the analysis because payment information may be incomplete for these patients. Controls with no diagnosis of MDD and no prescription for antidepressant or antipsychotic/antimanic drugs during the study years were selected using similar criteria.

For each study year, patients with MDD were matched 1-to-1 to controls using a combination of direct characteristic matching and propensity score analysis. Specifically, patients were matched directly by age, gender, region, insurance type, employment status, relationship to primary beneficiary, and Charlson Comorbidity Index[21,22] and by propensity score using a caliper of 0.25 standard deviations of the propensity score. The propensity score was calculated using a logistic regression with controls for the most frequently observed general physical comorbidities that were found to be statistically significantly different at baseline between MDD patients and controls and that were not known to be MDD related.[23–25] For example, we controlled for hypertension, which has no reported association with MDD, but did not control for back pain since we wanted to capture the incremental costs of this condition, which has been documented as MDD related (despite the ambiguity of the causal direction). Detailed comparisons of characteristics of MDD patients and controls before and after patient matching in both study years are presented in Supplementary eTables 2–5.

Direct Costs Estimation

Average costs per patient, including medical services and prescription drug costs, were calculated in the 2 study years for both MDD and control patients. Three categories of costs were estimated: (1) MDD costs, including costs that occurred on the same day and in the same location as a medical claim with an MDD diagnosis, as well as pharmaceutical costs for antidepressant and antipsychotic/antimanic drugs; (2) other depression costs, including medical costs that occurred on the same day and in the same location as a medical claim with a diagnosis for another type of depression but not MDD specifically, as well as pharmaceutical costs for antianxiety and anticonvulsant drugs; and (3) nondepression costs, including all costs not captured in the first 2 categories. Incremental costs were calculated in each study year by subtracting average costs of controls from those of MDD patients. While the first cost category was the basis for estimating the *direct costs of MDD*, attention to all 3 categories taken together yielded an estimate of the *direct costs of individuals with MDD*.

Direct costs were estimated according to employment and MDD treatment status: (1) employed and treated—costs estimated from claims data; (2) employed and not treated—MDD costs set equal to 0, and non-MDD costs (the second and third cost categories above) set equal to those incurred by employed and treated patients; and (3) not employed (treated or not treated)—costs assumed to be 1.7 times those found in the employed population based on the ratio of health care costs incurred by MDD patients in a Medicaid population compared with a privately insured population.[26] (See Supplementary eTable 6 for detailed calculation of ratios used to infer missing cost categories.) Since the direct costs of MDD for people aged ≥65 years could not be observed in these claims data, they were assumed equal to those calculated for individuals aged 50–64 years. Societal direct costs were extrapolated by multiplying NSDUH estimates of the number of people with MDD by the direct cost estimates per patient for each of these 3 categories, stratified by age and gender.

Suicide-Related Costs Estimation

Suicide-related costs were estimated using the human capital method, incorporating the conservative assumption that household services had no human capital value.[5,12] The total number of suicides by age and gender cohort in 2005 and 2010 was obtained from the Centers for Disease Control.[27] On the basis of prior literature, we attributed 50% of suicides to MDD in our cost model.[28–30] In addition, the present value of lifetime earnings was estimated based on mortality rates and life expectancies from the National Vital Statistics Report[31,32] together with data from the Bureau of Labor Statistics.[33,34] To express future earnings in present value terms, we applied a 3% discount rate.[35]

Workplace Costs Estimation

Workplace costs were estimated by assessing the value of missed days of work (absenteeism) and reduced productivity while at work (presenteeism) of individuals with MDD. By following the same approach as that described above for direct costs, workplace costs were estimated for the 3 categories: MDD costs, other depression costs, and nondepression costs. We estimated 3 categories of absenteeism costs: (1) injury/illness, (2) discretionary time off, and (3) disability. Absenteeism due to injury and illness was imputed for the employed and treated subgroup based on OptumHealth data, with outpatient visits on workdays counting as half

a day missed and inpatient or emergency department visits on workdays counting as full days missed. The second absenteeism cost category was based on NSDUH, which reported the number of workdays missed "because the respondent didn't want to be there." The added number of days missed by individuals with MDD compared with controls was attributed to the effects of MDD. Costs associated with these 2 categories were estimated for each patient based on the cumulative number of workdays missed (combining claims and NSDUH information) multiplied by that employee's daily wage (from claims data). The third category of absenteeism costs, disability, was estimated directly from the claims data, which included duration and costs of short- and long-term disability for employed and treated beneficiaries. Absenteeism costs in the employed and not-treated group were assumed to be 48% of those incurred by the employed and treated group based on the workdays missed reported by both groups (from NSDUH). Presenteeism costs were assessed at 6.1 times the cost of absenteeism due to injury and illness, following previous MDD literature estimates.[7] (See Supplementary eTable 6 for detailed calculation of ratios used to infer missing cost categories.) Finally, societal workplace costs were extrapolated using the approach described above for direct costs.

RESULTS

Prevalence, Employment, and Treatment Rates

Between 2005 and 2010, MDD prevalence rose from 13.8 million to 15.4 million adults (Table 1A). This growth was unevenly distributed by age, with the ≥ 50-year age group increasing fastest and the other age groups experiencing minor growth or slight decline (Figure 1). The overall change in prevalence was partly the result of the US adult population growing from 216 million to 228 million and partly due to an MDD prevalence rate increase from 6.4% to 6.8%.

Worsening economic conditions after the 2008 downturn took a particularly heavy toll, with 0.3 million fewer persons with MDD employed full-time, 0.3 million more employed part-time, and 1.6 million more not employed at all (ie, unemployed or not looking for work). Whereas the full-time

Table 1. Prevalence, Employment, and Treatment Rates of Major Depressive Disorder (MDD)[a]

A. Prevalence of adults with MDD in past year by employment status,[b] 2005 and 2010

	2005			2010			Change				
Status	All Adults	Adults With MDD	Prevalence Rate, %	All Adults	Adults With MDD	Prevalence Rate, %	Adults With MDD	Prevalence Rate, %	95% CI	*P* Value[c]	
Employed full-time	119,744,159	6,509,206	5.4	113,773,287	6,228,652	5.5	−280,553	0.04	0.03 to 0.04	<.001	
Employed part-time	28,204,055	1,984,965	7.0	32,961,178	2,317,097	7.0	332,132	−0.01	−0.02 to 0.00	.217	
Not employed	68,416,663	5,304,228	7.8	81,057,954	6,901,021	8.5	1,596,794	0.76	0.75 to 0.77	<.001	
Total	216,364,877	13,798,399	6.4	227,792,418	15,446,771	6.8	1,648,372	0.40	0.40 to 0.41	<.001	

B. Employment status of adults with and without MDD in past year,[b] 2005 and 2010

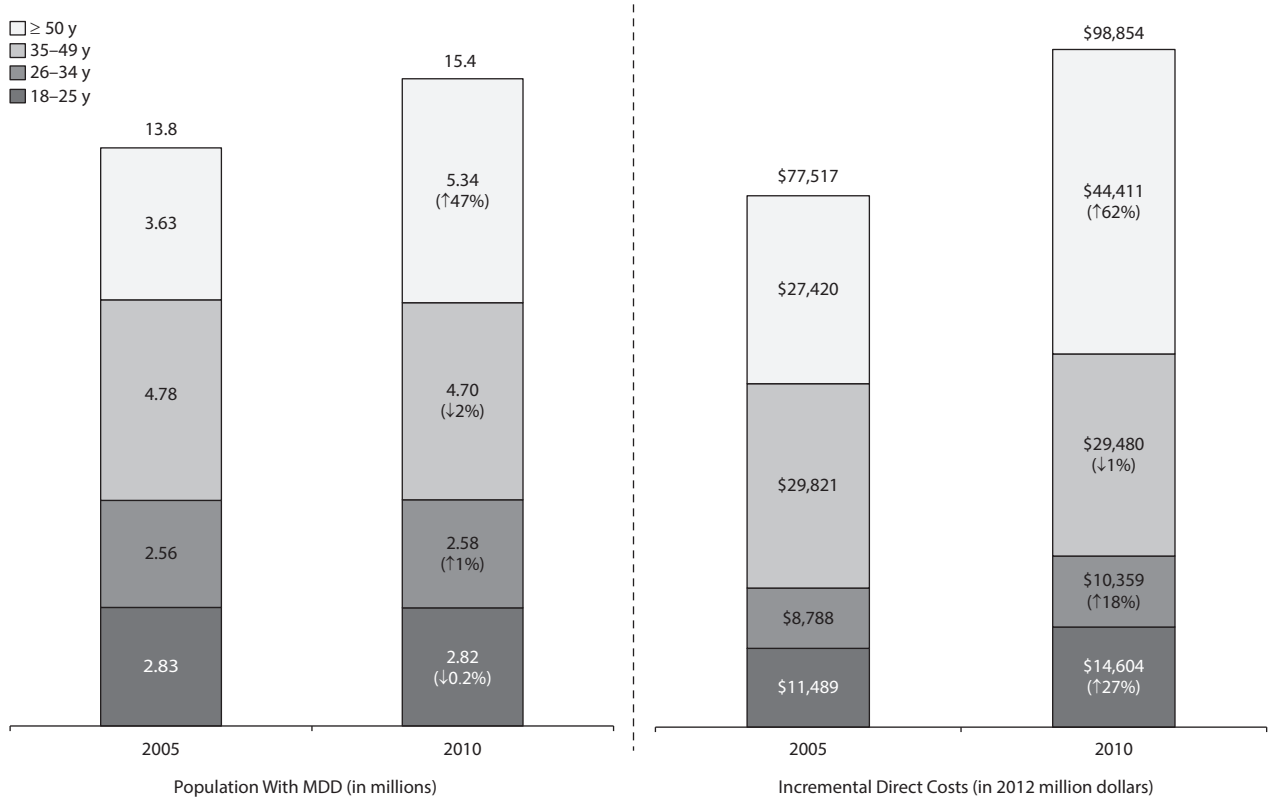
	2005			2010			Change in Adults With MDD			Change in Adults Without MDD		
Status	Adults With MDD, %	Adults Without MDD, %	Gap, %	Adults With MDD, %	Adults Without MDD, %	Gap, %	Change, %	95% CI	*P* Value[c]	Change, %	95% CI	*P* Value[c]
Employed full-time	47.2	55.9	−8.7	40.3	50.6	−10.3	−6.85	−6.89 to −6.81	<.001	−5.25	−5.26 to −5.24	<.001
Employed part-time	14.4	12.9	1.4	15.0	14.4	0.6	0.62	0.59 to 0.64	<.001	1.48	1.47 to 1.48	<.001
Not employed	38.4	31.2	7.3	44.7	34.9	9.8	6.24	6.20 to 6.27	<.001	3.78	3.77 to 3.79	<.001

C. Treatment rate of adults with MDD in past year by employment status,[b,d] 2005 and 2010

	2005		2010		Change	
Status	No. of Treated Cases	Rate, %	No. of Treated Cases	Rate, %	No. of Treated Cases	Rate, %
Employed full-time	2,951,386	45.6	3,216,593	51.8	265,206	6.1
Employed part-time	956,957	48.5	1,147,033	49.6	190,076	1.2
Not employed	3,267,970	61.6	4,310,542	62.5	1,042,572	0.8
Total	7,176,313	52.2	8,674,168	56.2	1,497,854	4.0

[a]Data source: US Department of Health and Human Services. National Survey on Drug Use and Health, public-use files, 2005[13] and 2010.[14]
[b]In 2005 and 2010, MDD in past year is based on the variables AJAMDDEYR ("adult: adjusted past-year major depressive episode") and AMDDEYR ("adult: past-year major depressive episode"), respectively. Employment status is based on the variable EMPSTAT4 ("imputation revised employment status 18+"). Results are weighted based on the variable ANALWT_C ("final person-level sample weight"). Adults with unknown MDD status were excluded from analysis.
[c]*P* values for the change across years are calculated using the 2-sample *z* test for independent proportions.
[d]In 2005 and 2010, treatment rate is identified based on the variable AMHTXRC3 ("received any mental health treatment in past year").

Figure 1. Prevalence and Cost of Individuals With Major Depressive Disorder (MDD) by Age Group



employment rate was 8.7 percentage points lower for persons with than those without MDD in 2005, this gap widened to 10.3 percentage points in 2010 (Table 1B). Furthermore, full-time employment rates in the MDD group decreased 6.9 percentage points during this period, from 47.2% to 40.3%. This represented both a lower starting level and a steeper decline compared with the non-MDD group, which experienced a 5.3 percentage point reduction from 55.9% to 50.6%. Compared with the non-MDD group, the MDD group was also more frequently unemployed or not looking for work. Taken together, following the economic downturn, the "not-employed" rate increased by 6.2 percentage points among those with MDD compared with 3.8 percentage points within the non-MDD group.

There were 1.5 million more people treated for MDD in 2010 than in 2005, with the treatment rate increasing from 52.2% to 56.2% in that period (Table 1C). While the rate of treatment increased by 6.1 percentage points among the full-time employed, less pronounced rates of increase were observed among the part-time employed and the not-employed groups (1.2 and 0.8 percentage points, respectively).

MDD Costs: 2010 Versus 2005

The incremental economic burden of individuals with MDD was $173.2 billion in 2005 and $210.5 billion in 2010, an increase of 21.5% over this period (Table 2A). A large portion of this increase was attributable to higher direct medical and presenteeism costs. The composition of total incremental costs was stable over time, with 48%–50% attributable to workplace costs, 45%–47% to direct costs, and 5% to suicide-related costs. Of these total incremental costs, only 38% was attributable to MDD itself as opposed to comorbid conditions (Table 2B).

Direct costs. Direct costs incurred by individuals with MDD totaled $77.5 billion in 2005, rising 27.5% to $98.9 billion in 2010 (Table 2A). The majority of the costs were for outpatient and inpatient medical services representing 15%–18% and 9%–10% of total costs in each study year, respectively. In addition, pharmacy costs accounted for 15% of the total in 2005 and 13% in 2010. Furthermore, direct costs attributable to individuals with MDD aged ≥ 50 years increased the fastest, the costs incurred by 18- to 25- and 26- to 34-year-old patients grew less rapidly, while those stemming from the 35- to 49-year age group remained flat (Figure 1). (See Supplementary eTable 7 for additional results on incremental direct costs of individuals with MDD by employment status, treatment status, and age group in 2005 and 2010.)

For employed and treated patients, incremental direct costs of health care services were $5,707 per MDD patient in 2005, increasing by 5% in 2010 to $5,988 (Table 3). In both study years, the costs of services that were directly attributable to MDD accounted for only 40% of the incremental direct costs, with MDD drug costs declining over time as generics became more widely used.[36] An additional 10%–11% was due to depression other than MDD, with another 48%–51% stemming from other conditions (eg, hospitalization or

Table 2. Incremental Economic Burden of Individuals With Major Depressive Disorder (MDD) in 2005 and 2010 (all costs and costs of MDD alone, in 2012 dollars)

Type of Cost	2005 Dollars (in millions)	2005 Percentage of Total	2010 Dollars (in millions)	2010 Percentage of Total	2005 to 2010 Change in Dollars, %
A. Incremental economic burden of individuals with MDD					
Direct costs	$77,517	45	$98,854	47	27.5
Medical services	$50,828	29	$70,736	34	39.2
Outpatient	$26,803	15	$38,205	18	42.5
Inpatient	$14,784	9	$20,598	10	39.3
Emergency department	$3,647	2	$4,934	2	35.3
Other medical services	$5,595	3	$6,999	3	25.1
Pharmaceutical services	$26,689	15	$28,117	13	5.4
Suicide-related costs	$9,435	5	$9,691	5	2.7
Workplace costs	$86,268	50	$102,003	48	18.2
Absenteeism	$21,537	12	$23,331	11	8.3
Presenteeism	$64,731	37	$78,672	37	21.5
Total	$173,220	100	$210,548	100	21.5
B. Incremental economic burden of MDD					
Direct costs	$21,579	33	$27,688	34	28.3
Medical services	$12,147	18	$16,647	21	37.0
Outpatient	$7,282	11	$10,097	13	38.7
Inpatient	$3,790	6	$4,878	6	28.7
Emergency department	$84	0	$161	0	91.8
Other medical services	$991	1	$1,512	2	52.5
Pharmaceutical services	$9,432	14	$11,041	14	17.1
Suicide-related costs	$9,435	14	$9,691	12	2.7
Workplace costs	$35,251	53	$42,997	53	22.0
Absenteeism	$8,306	13	$9,263	12	11.5
Presenteeism	$26,945	41	$33,734	42	25.2
Total	$66,265	100	$80,377	100	21.3

physician office visits for mental illnesses, including anxiety, adjustment disorder, and posttraumatic stress disorder, as well as a range of non–mental health services). This was mostly composed of various manifestations of pain, including disc and back disorders, abdominal pain, and chest pain, as well as sleep disorders, and migraines (Table 3).[37,38] (See Supplementary eTable 8 for additional results on incremental cost per patient for non–mental health medical services in 2010.)

Suicide-related costs. The adult suicide rate was 14.2 per 100,000 in 2005 and 15.9 per 100,000 in 2010,[27] with 50% of those suicides attributed to MDD. Suicide-related costs for the MDD group were estimated at $9.4 billion in 2005, 5% of the overall economic burden, rising by 2.7% to $9.7 billion in 2010 (Table 2). (See Supplementary eTable 9 for the number of suicides and a detailed calculation of lifetime earnings lost due to MDD in 2005 and 2010.)

Workplace costs. Presenteeism accounted for approximately 3 quarters of workplace costs and represented 37% of the overall economic burden of individuals with MDD (Table 2). In each study year, the equivalent of approximately 32 incremental workdays was lost due to presenteeism by the average individual with MDD (data not shown). Total presenteeism costs were estimated at $64.7 billion in 2005, and rose 21.5% over the ensuing 5 years to $78.7 billion in 2010. In contrast, incremental costs associated with absenteeism grew only 8.4% over the period 2005 to 2010, from $21.5 billion to $23.3 billion. This is composed of 21.5% growth in absenteeism due to injury/illness costs, 19.4% growth in discretionary absenteeism costs, and 24.6% decrease in disability costs. (See Supplementary eTable 10 for detailed results on the incremental workplace costs of individuals with MDD in 2005 and 2010.)

DISCUSSION

The purpose of this study was to estimate the economic burden of people with MDD; assess the cost share attributable to MDD versus comorbid conditions; understand the relative contributions of direct costs, suicide-related costs, and workplace costs; and analyze changes in these cost categories between 2005 and 2010. The emphasis on understanding the role of comorbid conditions dates back to our earlier cost-of-illness study,[5] which concluded that "future research will incorporate additional costs associated with depression sufferers, including the excess costs of their coexisting psychiatric and medical conditions."[5(p1465)]

The current study adds to our understanding of MDD as a source of significant economic burden. We estimated the incremental cost of people with MDD at $173.2 billion in 2005 and $210.5 billion in 2010, with 45%–47% attributable to direct costs, 5% to suicide-related costs, and 48%–50% to workplace costs. But MDD direct costs (including both medical and pharmaceutical services directly related to MDD treatment itself) accounted for only 12%–13% of this incremental burden of people with MDD, totaling $21.6 billion in 2005 and $27.7 billion in 2010. In fact, for every dollar spent on MDD direct costs in 2010, an additional $1.90 was spent on MDD-related indirect costs (ie, suicide-related, workplace), and another $4.70 was spent on direct and workplace comorbidity costs incurred by persons with MDD (Figure 2).

Table 3. Direct Incremental Cost of Employed and Treated MDD Patients, 2005 and 2010 (in 2012 dollars)[a]

	2005				2010			
Cost Category	Cost Per Patient With MDD	Cost Per Patient Without MDD	Incremental Cost Per Patient[b]	Percentage of Total Incremental Cost	Cost Per Patient With MDD	Cost Per Patient Without MDD	Incremental Cost Per Patient[b]	Percentage of Total Incremental Cost
MDD costs	$2,294	$0	$2,294	40	$2,366	$0	$2,366	40
Medical services	$1,264	$0	$1,264	22	$1,410	$0	$1,410	24
Inpatient	$387	$0	$387	7	$411	$0	$411	7
Emergency department	$8	$0	$8	0	$14	$0	$14	0
Outpatient	$773	$0	$773	14	$865	$0	$865	14
Other	$96	$0	$96	2	$121	$0	$121	2
Prescription drug	$1,030	$0	$1,030	18	$955	$0	$955	16
Antidepressants	$783	$0	$783	14	$584	$0	$584	10
Antipsychotics/antimanics	$248	$0	$248	4	$371	$0	$371	6
Other depression costs	$675	$30	$645	11	$620	$35	$584	10
Medical services	$412	$12	$400	7	$470	$14	$456	8
Inpatient	$159	$1	$157	3	$160	$4	$156	3
Emergency department	$22	$0	$22	0	$35	$1	$34	1
Outpatient	$197	$10	$187	3	$231	$9	$222	4
Other	$35	$0	$34	1	$44	$0	$44	1
Prescription drug	$263	$18	$246	4	$150	$21	$128	2
Antianxiety agents	$49	$1	$48	1	$25	$1	$24	0
Anticonvulsants	$214	$16	$198	3	$124	$20	$104	2
Nondepression costs	$6,679	$3,911	$2,767	48	$7,394	$4,356	$3,038	51
Other mental health disorders	$436	$37	$399	7	$594	$70	$524	9
Inpatient	$171	$15	$156	3	$183	$37	$147	2
Emergency department	$32	$3	$29	1	$51	$7	$44	1
Outpatient	$140	$17	$123	2	$234	$25	$209	3
Other	$92	$1	$91	2	$126	$2	$124	2
Non–mental health disorders[c]	$4,595	$3,083	$1,512	26	$5,130	$3,382	$1,748	29
Inpatient	$1,322	$951	$371	6	$1,552	$1,053	$499	8
Emergency department	$271	$131	$140	2	$316	$171	$145	2
Outpatient	$2,714	$1,839	$874	15	$3,029	$2,017	$1,012	17
Other	$289	$162	$127	2	$233	$141	$91	2
Prescription drug	$1,647	$792	$856	15	$1,671	$904	$767	13
Analgesics—opioid	$151	$7	$145	3	$137	$13	$124	2
Ulcer drugs	$169	$62	$107	2	$115	$45	$71	1
Hypnotics	$87	$4	$83	1	$57	$4	$54	1
ADHD/antinarcolepsy/ antiobesity/anorexiants	$119	$4	$115	2	$171	$9	$162	3
Other nondepression prescription drugs	$1,121	$714	$407	7	$1,189	$833	$356	6
Total direct costs	$9,648	$3,941	$5,707	100	$10,379	$4,391	$5,988	100

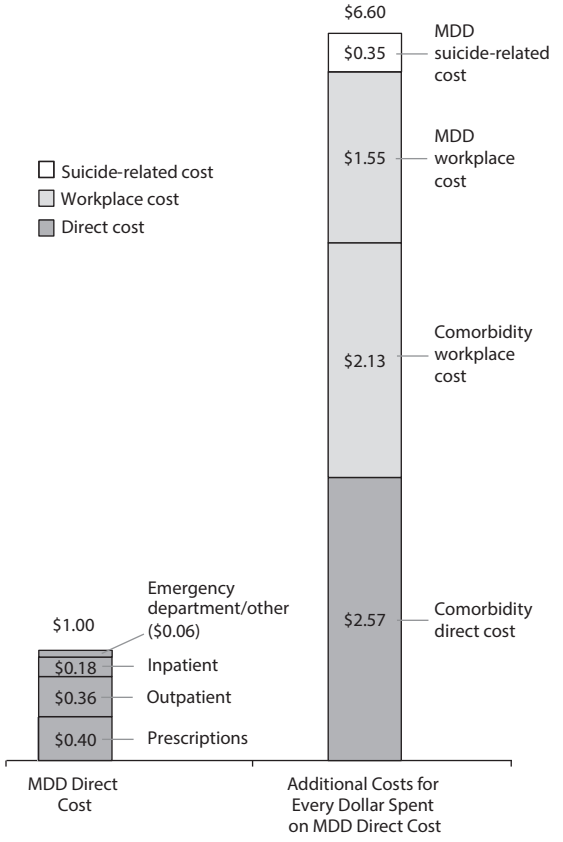
[a]Data source: OptumHealth Reporting and Insights.[19,20]
[b]All differences were statistically significant with *P* values < .001 (based on Wilcoxon signed rank tests).
[c]Top *ICD-9* codes in both years include 722 (intervertebral disc disorders); 723 (other disorders of cervical region [eg, cervicalgia]); 724 (other and unspecified disorders of back [eg, lumbago]); 780 (general symptoms [eg, sleep disturbances, malaise, and fatigue]); 786 (symptoms involving respiratory system and other chest symptoms [eg, chest pain]); and 789 (other symptoms involving abdomen and pelvis [eg, abdominal pain]).

Individuals with MDD thereby experience a wide range of disease burdens, much of which is not usually categorized as directly related to the MDD treatment itself. The treatment rate of MDD remained relatively low in 2005 and 2010 (in the 50% range), likely contributing to the increasing burden of the disease. Thus, to the extent there is success in raising treatment rates, we would expect a shift from costs of people with the disease (ie, reduced cost of comorbid conditions) to costs associated with MDD (ie, increased treatment costs). The extent to which these competing forces would offset one another in dollar terms is a topic for further research. For example, whereas a condition like back pain may well be exacerbated by the presence of depression and therefore could potentially be alleviated by its successful treatment, the same is unlikely to be true for a condition like hypertension or cancer. Recent studies[39–41] suggest that collaborative care approaches that are mindful of these different pathways could allow for cost savings in the long term.

Understanding the source of cost changes between 2005 and 2010 reported in this study also merits further attention. The 27.5% increase in direct costs for people with MDD can be broken into 2 approximately equal-sized components: change in number of MDD cases, accounting for 12.8 percentage points of the increase in direct cost (of which 5.8 percentage points are due to growth in the adult US population, and 7.0 percentage points are attributable to an increase in the MDD prevalence rate) (Table 1); and change in cost per case, accounting for an additional 14.8 percentage points of the increase in direct costs.

Further research on the underlying drivers of these observed changes is warranted.[42] Indeed, the increase in the incremental direct cost per employed and treated patient

Figure 2. Additional Costs of Individuals With Major Depressive Disorder (MDD) for Every Dollar Spent on MDD Direct Cost in 2010



with MDD reported in Table 3 was more modest among the employed and treated patients with MDD, at 5%. This was most likely driven by the changing mix of employed patients with MDD in 2010 compared with 2005. That is, the worsening economy most likely led to a less severely depressed employed group by 2010, which would be an offsetting factor affecting the cost change for this group.

Through the business cycle, labor force attachment is far more volatile for people with MDD compared to those without. On the one hand, involuntary unemployment could spur more MDD, and on the other hand, the symptoms of illness could diminish employment prospects.[43] In economically robust times, persons with MDD tend to be highly employable, but when economic conditions worsen, they are disproportionately adversely affected, especially those aged 50 years and older. Furthermore, during economic downturns, the buffer of part-time work is not as widely available or accessed by the MDD group. Thus, the complex interplay of work status, MDD symptoms, and MDD treatment warrants continued study. Shining a bright light on the relative impact of these different contributors to direct cost changes, and understanding how they have moved historically, would offer insight into the available levers that could be brought to bear in most effectively managing resource utilization in this context over time.

There are several limitations of this study that are noteworthy. First, in the absence of a single data source to evaluate the economic burden of MDD, we relied on both original as well as literature-based estimates. Our ability to overlay literature-based estimates on our original analyses depends on the underlying consistency of these sources. However, it is comforting that many of these estimates are based on representative samples of persons with MDD drawn from the same or similar time periods and that the results do not appear to be highly sensitive to changes in these estimates. That is, we performed a sensitivity analysis with respect to the 3 parameters that are drawn from estimates in the literature (ie, the direct costs of MDD subjects who are not employed, the absenteeism costs of MDD subjects who are employed but not treated, and the presenteeism costs of MDD subjects who are employed) and found that increasing (or decreasing) these parameters by 10% results in an increase (or decrease) in the overall costs of MDD of 6% and in the costs of people with MDD of 5%. Second, presenteeism is estimated based on the relationship between presenteeism and absenteeism costs in 2002. To the extent this ratio changed through the business cycle, our estimate may not properly capture the workplace dynamic. Also, by 2010 many more jobs did not require a physical presence in the workplace, which could have changed the relationship between absenteeism and presenteeism relative to an earlier era. Third, our data do not allow costs for patients aged 65 years and older to be estimated directly, and so we have imputed these costs based on the cohort aged 50–64 years. In addition, our data do not allow for analysis of beneficiaries covered under certain types of managed care plans. This raises the possibility that our extrapolation does not fully reflect the experiences of these individuals. Finally, there are no severity markers in the data on which this study is based. Further research is needed on the sources of the economic burden of depression by severity of illness.

Taken together, the economic burden of adults with MDD is large and has grown over time. Several factors most likely contributed to the increase in costs between 2005 and 2010, including growth in the US population, increase in MDD prevalence, increase in treatment cost per individual with MDD, changes in employment and treatment rates, as well as changes in the composition and quality of MDD treatment services. Future research should focus on the relative importance of these different factors and analyze further the comorbidities associated with MDD that account for the largest portion of the total economic burden of the disease.

Author affiliations: Harvard Medical School (Dr Kessler) and Analysis Group, Inc (Mr Greenberg and Mss Fournier, Sisitsky, and Pike), Boston, Massachusetts.
Potential conflicts of interest: In the past 12 months, **Dr Kessler** has served as a consultant for Hoffmann-La Roche and Johnson & Johnson Wellness and Prevention; has served on advisory boards for Mensante, Johnson & Johnson Services, Lake Nona Life Project, and US Preventive Medicine; and owns 25% share in DataStat. **Mr Greenberg** and **Mss Fournier**, **Sisitsky**, and **Pike** have no financial conflicts of interest to disclose.
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Supplementary Material

Article Title: The Economic Burden of Adults With Major Depressive Disorder in the United States (2005 and 2010)

Author(s): Paul E. Greenberg, MS, MA; Andree-Anne Fournier, MA; Tammy Sisitsky, MA; Crystal T. Pike, MBA; and Ronald C. Kessler, PhD

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List of Supplementary Material for the article

Supplementary eTable 1. Framework for evaluation of the economic burden of adults with MDD in the United States (2005 and 2010)

MDD population employment/treatment status		Direct costs	Indirect costs		
			Suicide-related costs	Workplace costs	
				Absenteeism/disability costs	Presenteeism costs
Employed	**Treated**	• Annual MDD costs, other depression costs, and non-depression costs per individual with MDD estimated based on medical and pharmaceutical claims data in privately insured population (OptumHealth Reporting and Insights) • Societal costs extrapolated using prevalence estimate from National Survey on Drug Use and Health (NSDUH)	• Total number of suicides based on national death statistics in National Center for Injury Prevention and Control, CDC • MDD-related suicides assumed to account for 50% of all suicides based on literature • Present value of lifetime earnings estimated based on mortality rates and life expectancies from National Vital Statistics Reports as well as national wage data from Bureau of Labor Statistics	• Days missed due to illness/injury estimated based on medical services utilized on work days using claims data in privately insured population; associated costs per individual with MDD per year estimated based on salary information in the database (OptumHealth Reporting and Insights) • Annual days missed due to reasons other than illness/injury per individual with MDD estimated based on NSDUH; associated costs inferred based on estimate of cost per missed day due to illness/injury (OptumHealth Reporting and Insights) • Disability costs per individual with MDD per year estimated based on OptumHealth Reporting and Insights claims data • Societal costs extrapolated using prevalence estimate from NSDUH	• Societal costs inferred based on ratio of presenteeism to absenteeism costs estimated in Stewart et al., 2003 (See Supplementary eTable 6)
	Not treated	• MDD costs set equal to zero • Other depression and non-depression costs per individual with MDD per year set equal to those incurred by employed and treated patients • Societal costs extrapolated using prevalence estimate from NSDUH		• Days missed and associated costs inferred based on estimates for treated population and ratio of days missed for not treated to treated individual with MDD based on NSDUH (See Supplementary eTable 6) • Societal costs extrapolated using prevalence estimate from NSDUH	
Not employed	**Treated**	• Annual MDD costs, other depression costs, and non-depression costs per individual with MDD inferred based on cost estimates for employed MDD individuals and ratio of Medicaid to privately insured cost estimates from Ivanova et al., 2011 (See Supplementary eTable 6) • Societal costs extrapolated using prevalence estimate from NSDUH		N/A	
	Not treated				

Original estimates

Inferred estimates

Supplementary eTable 2. Comparison of MDD patients and controls in administrative claims data before patient matching, 2005[a]

Characteristics	MDD patients (N=37,791)		Controls (N=1,038,655)		P-value[b]	
Demographics						
Age, mean (SD)	44.4	(11.44)	43.3	(12.63)	<0.001	*
Gender, n (%) male	12,106	(32.0%)	538,438	(51.8%)	<0.001	*
Region, n (%)						
South	15,451	(40.9%)	438,513	(42.2%)	<0.001	*
Midwest	8,759	(23.2%)	242,179	(23.3%)	0.530	
West	5,504	(14.6%)	153,013	(14.7%)	0.367	
Northeast	7,952	(21.0%)	201,121	(19.4%)	<0.001	*
Other	125	(0.3%)	3,829	(0.4%)	0.232	
Insurance type, n (%)						
PPO	21,002	(55.6%)	613,732	(59.1%)	<0.001	*
POS	11,366	(30.1%)	281,238	(27.1%)	<0.001	*
Indemnity	3,799	(10.1%)	89,166	(8.6%)	<0.001	*
Other	1,624	(4.3%)	54,519	(5.2%)	<0.001	*
Employment status, n (%)						
Actively employed	28,026	(74.2%)	828,841	(79.8%)	<0.001	*
Retired	2,736	(7.2%)	71,246	(6.9%)	0.004	*
Other	7,029	(18.6%)	138,568	(13.3%)	<0.001	*
Relationship to primary beneficiary, n (%)						
Self	22,225	(58.8%)	631,065	(60.8%)	<0.001	*
Spouse	13,195	(34.9%)	329,353	(31.7%)	<0.001	*
Child	2,260	(6.0%)	75,970	(7.3%)	<0.001	*
Other	111	(0.3%)	2,267	(0.2%)	0.002	*
Charlson Comorbidity Index (CCI), mean (SD)[c]	0.53	(1.13)	0.27	(0.73)	<0.001	*
General physical comorbidities,[c] n (%)						
Hypertension	8,996	(23.8%)	201,655	(19.4%)	<0.001	*
Hypothyroidism	3,854	(10.2%)	50,568	(4.9%)	<0.001	*
Deficiency anemias	2,371	(6.3%)	30,006	(2.9%)	<0.001	*
Rheumatoid arthritis	1,393	(3.7%)	14,575	(1.4%)	<0.001	*
Neurological disorders	1,612	(4.3%)	10,444	(1.0%)	<0.001	*
Cardiac arrhythmias	1,263	(3.3%)	20,301	(2.0%)	<0.001	*
Valvular disease	1,262	(3.3%)	20,003	(1.9%)	<0.001	*
Fluid and electrolyte disorders	1,473	(3.9%)	11,823	(1.1%)	<0.001	*
Mental comorbidities,[d] n (%)						
Anxiety disorders	10,464	(27.7%)	13,913	(1.3%)	<0.001	*
Adjustment disorders	3,751	(9.9%)	13,350	(1.3%)	<0.001	*
Sleep disorders	3,662	(9.7%)	20,053	(1.9%)	<0.001	*
Mood disorders	3,697	(9.8%)	940	(0.1%)	<0.001	*
Miscellaneous other mental disorders	1,942	(5.1%)	8,065	(0.8%)	<0.001	*
ADD	1,425	(3.8%)	3,965	(0.4%)	<0.001	*
Alcohol abuse	1,479	(3.9%)	2,710	(0.3%)	<0.001	*
Screening for disorders	1,217	(3.2%)	10,050	(1.0%)	<0.001	*
Drug abuse	1,253	(3.3%)	1,197	(0.1%)	<0.001	*
Schizophrenia	1,003	(2.7%)	586	(0.1%)	<0.001	*
Sexual and gender identity disorders	999	(2.6%)	17,603	(1.7%)	<0.001	*
Drug use,[e] n (%)						
Antidepressants	30,441	(80.6%)	0	(0.0%)	<0.001	*
Antipsychotics	6,288	(16.6%)	0	(0.0%)	<0.001	*
Antimanics	915	(2.4%)	0	(0.0%)	<0.001	*
Medical resource use, mean (SD)						
Inpatient visits	0.44	(1.56)	0.09	(0.40)	<0.001	*
Inpatient days	1.98	(8.93)	0.33	(2.70)	<0.001	*
Rehab facility visits	0.07	(0.83)	0.00	(0.19)	<0.001	*
Rehab facility days	0.33	(3.68)	0.02	(1.07)	<0.001	*
Emergency department visits	0.74	(2.46)	0.27	(0.89)	<0.001	*
Outpatient visits	23.41	(18.15)	6.98	(8.54)	<0.001	*
Other visits	2.88	(6.39)	1.29	(3.26)	<0.001	*
Total direct costs,[f] mean (SD)	$12,701	($27,637)	$3,813	($12,587)	<0.001	*
Medical service costs	$9,273	($26,261)	$3,087	($12,093)	<0.001	*
Inpatient	$3,591	($21,298)	$1,024	($9,085)	<0.001	*
Emergency department	$426	($1,819)	$133	($802)	<0.001	*
Outpatient	$4,621	($9,230)	$1,764	($5,866)	<0.001	*
Other	$635	($3,858)	$166	($2,139)	<0.001	*
Prescription drug	$3,428	($5,535)	$726	($2,333)	<0.001	*

Supplementary eTable 2. Comparison of MDD patients and controls in administrative claims data before patient matching, 2005[a]

Characteristics	MDD patients (N=37,791)		Controls (N=1,038,655)		P-value[b]	
MDD costs,[f] mean (SD)	$2,480	($4,812)	$0	($0)	<0.001	*
Medical service costs	$1,399	($4,324)	$0	($0)	<0.001	*
Inpatient	$478	($3,251)	$0	($0)	<0.001	*
Emergency department	$10	($169)	$0	($0)	<0.001	*
Outpatient	$810	($1,838)	$0	($0)	<0.001	*
Other	$101	($1,407)	$0	($0)	<0.001	*
Prescription drug	$1,081	($1,631)	$0	($0)	<0.001	*
GPI 58 (Antidepressants)	$805	($993)	$0	($0)	<0.001	*
GPI 59 (Antipsychotics/Antimanic Agents)	$276	($1,122)	$0	($0)	<0.001	*
Other depression costs,[f] mean (SD)	$773	($2,751)	$23	($730)	<0.001	*
Medical service costs	$468	($2,531)	$11	($696)	<0.001	*
Inpatient	$191	($1,920)	$2	($674)	<0.001	*
Emergency department	$26	($296)	$0	($20)	<0.001	*
Outpatient	$210	($980)	$9	($163)	<0.001	*
Other	$41	($807)	$0	($30)	<0.001	*
Prescription drug	$305	($897)	$13	($213)	<0.001	*
GPI 57 (Antianxiety Agents)	$54	($269)	$1	($27)	<0.001	*
GPI 72 (Anticonvulsants)	$250	($833)	$11	($210)	<0.001	*
Non-depression costs,[f] mean (SD)	$9,448	($26,116)	$3,789	($12,550)	<0.001	*
Other mental health disorders	$573	($3,973)	$46	($1,259)	<0.001	*
Outpatient	$158	($825)	$17	($271)	<0.001	*
Inpatient	$272	($3,245)	$22	($1,179)	<0.001	*
Emergency department	$44	($409)	$4	($120)	<0.001	*
Rehab	$71	($1,140)	$2	($149)	<0.001	*
Other	$29	($670)	$1	($250)	<0.001	*
Non-mental health disorders	$6,833	($24,411)	$3,030	($11,912)	<0.001	*
Outpatient	$3,443	($8,613)	$1,739	($5,848)	<0.001	*
Inpatient	$2,650	($20,022)	$1,000	($8,904)	<0.001	*
Emergency department	$347	($1,617)	$128	($789)	<0.001	*
Rehab	$7	($201)	$2	($122)	<0.001	*
Other	$386	($3,081)	$161	($2,068)	<0.001	*
Prescription drug	$2,042	($4,673)	$713	($2,315)	<0.001	*
GPI 65 (Analgesics - Opioid)	$189	($1,881)	$7	($271)	<0.001	*
GPI 49 (Ulcer Drugs)	$194	($519)	$57	($265)	<0.001	*
GPI 60 (Hypnotics)	$96	($288)	$4	($46)	<0.001	*
GPI 61 (Adhd/Anti-Narcolepsy/Anti-Obesity/Anorexiants)	$127	($559)	$4	($83)	<0.001	*
Other non-depression related prescription drugs	$1,436	($3,816)	$641	($2,239)	<0.001	*
Workloss data						
	(N=9,644)		(N=343,002)			
Days of missed work, mean (SD)						
Total missed days	24.28	(50.71)	4.74	(13.01)	<0.001	*
Absenteeism days	11.87	(10.18)	3.86	(4.70)	<0.001	*
MDD absenteeism days	4.29	(5.14)	0.00	(0.00)	<0.001	*
Other depression absenteeism days	1.03	(3.00)	0.07	(0.89)	<0.001	*
Non-depression absenteeism days	6.55	(7.63)	3.79	(4.60)	<0.001	*
Disability days	12.41	(52.11)	0.88	(12.18)	<0.001	*
Costs of missed work, mean (SD)						
Total indirect costs	$4,350	($6,836)	$1,166	($2,212)	<0.001	*
Absenteeism costs	$2,989	($3,356)	$1,069	($1,715)	<0.001	*
MDD absenteeism costs	$1,126	($1,899)	$0	($0)	<0.001	*
Other depression absenteeism costs	$270	($952)	$21	($336)	<0.001	*
Non-depression absenteeism costs	$1,593	($2,100)	$1,048	($1,670)	<0.001	*
Disability costs	$1,361	($6,461)	$97	($1,396)	<0.001	*

Notes:

[a] Data source: OptumHealth Reporting and Insights[19,20].

[b] P-values were calculated using chi-squared tests for categorical variables and Wilcoxon rank sum tests for continuous variables. P-values <0.05 are indicated with an asterisk ("*").

[c] The 17 conditions included in the CCI were identified using ICD-9-CM diagnosis codes reported by Quan et al., 2005 [21] .

[d] Mental comorbidities were identified using ICD-9-CM diagnosis codes.

[e] Drugs were identified using the first two digits of the Generic Product Identifier (GPI).

[f] Costs reflect all costs paid for the service including patient out-of-pocket costs. Costs were inflated to 2012 USD using the medical care component of the Consumer Price Index.

Supplementary eTable 3. Comparison of MDD patients and controls in administrative claims data before patient matching, 2010[a]

Characteristics	MDD patients (N=50,197)		Controls (N=1,411,443)		P-value[b]	
Demographics						
Age, mean (SD)	45.0	(12.15)	43.2	(12.99)	<0.001	*
Gender, n (%) male	17,261	(34.4%)	734,628	(52.0%)	<0.001	*
Region, n (%)						
South	12,403	(24.7%)	436,067	(30.9%)	<0.001	*
Midwest	12,637	(25.2%)	371,907	(26.3%)	<0.001	*
West	7,621	(15.2%)	238,079	(16.9%)	<0.001	*
Northeast	15,803	(31.5%)	342,568	(24.3%)	<0.001	*
Other	1,733	(3.5%)	22,822	(1.6%)	<0.001	*
Insurance type, n (%)						
PPO	33,276	(66.3%)	944,185	(66.9%)	0.005	*
POS	9,463	(18.9%)	286,164	(20.3%)	<0.001	*
Indemnity	5,919	(11.8%)	130,545	(9.2%)	<0.001	*
Other	1,539	(3.1%)	50,549	(3.6%)	<0.001	*
Employment status, n (%)						
Actively employed	40,284	(80.3%)	1,223,802	(86.7%)	<0.001	*
Retired	4,307	(8.6%)	87,859	(6.2%)	<0.001	*
Other	5,606	(11.2%)	99,782	(7.1%)	<0.001	*
Relationship to primary beneficiary, n (%)						
Self	28,599	(57.0%)	874,316	(61.9%)	<0.001	*
Spouse	17,800	(35.5%)	418,408	(29.6%)	<0.001	*
Child	3,670	(7.3%)	116,013	(8.2%)	<0.001	*
Other	128	(0.3%)	2,706	(0.2%)	0.002	*
Charlson Comorbidity Index (CCI), mean (SD)[c]	0.90	(2.25)	0.41	(1.28)	<0.001	*
General physical comorbidities,[c] n (%)						
Hypertension	13,826	(27.5%)	295,285	(20.9%)	<0.001	*
Hypothyroidism	6,481	(12.9%)	87,561	(6.2%)	<0.001	*
Deficiency anemias	4,708	(9.4%)	61,551	(4.4%)	<0.001	*
Rheumatoid arthritis	2,586	(5.2%)	28,132	(2.0%)	<0.001	*
Neurological disorders	4,200	(8.4%)	27,582	(2.0%)	<0.001	*
Cardiac arrhythmias	3,240	(6.5%)	43,273	(3.1%)	<0.001	*
Valvular disease	2,037	(4.1%)	30,331	(2.1%)	<0.001	*
Fluid and electrolyte disorders	2,742	(5.5%)	23,595	(1.7%)	<0.001	*
Mental comorbidities,[d] n (%)						
Anxiety disorders	18,637	(37.1%)	29,615	(2.1%)	<0.001	*
Adjustment disorders	7,269	(14.5%)	21,646	(1.5%)	<0.001	*
Sleep disorders	5,134	(10.2%)	24,463	(1.7%)	<0.001	*
Mood disorders	7,367	(14.7%)	3,444	(0.2%)	<0.001	*
Miscellaneous other mental disorders	3,614	(7.2%)	11,811	(0.8%)	<0.001	*
ADD	4,865	(9.7%)	11,222	(0.8%)	<0.001	*
Alcohol abuse	3,588	(7.1%)	6,208	(0.4%)	<0.001	*
Screening for disorders	2,484	(4.9%)	21,667	(1.5%)	<0.001	*
Drug abuse	3,253	(6.5%)	5,151	(0.4%)	<0.001	*
Schizophrenia	2,359	(4.7%)	2,003	(0.1%)	<0.001	*
Sexual and gender identity disorders	1,783	(3.6%)	28,214	(2.0%)	<0.001	*
Drug use,[e] n (%)						
Antidepressants	38,401	(76.5%)	0	(0.0%)	<0.001	*
Antipsychotics	9,347	(18.6%)	0	(0.0%)	<0.001	*
Antimanics	1,037	(2.1%)	0	(0.0%)	<0.001	*
Medical resource use, mean (SD)						
Inpatient visits	0.49	(1.67)	0.12	(0.58)	<0.001	*
Inpatient days	2.65	(11.62)	0.48	(3.51)	<0.001	*
Emergency department visits	0.69	(2.00)	0.31	(1.02)	<0.001	*
Outpatient visits	24.49	(19.28)	7.64	(9.50)	<0.001	*
Other visits	2.74	(6.12)	1.06	(2.85)	<0.001	*
Total direct costs,[f] mean (SD)	$13,884	($54,123)	$3,913	($13,295)	<0.001	*
Medical service costs	$10,733	($53,285)	$3,157	($12,512)	<0.001	*
Inpatient	$4,442	($49,702)	$1,015	($9,174)	<0.001	*
Emergency department	$520	($2,397)	$165	($840)	<0.001	*
Outpatient	$5,111	($13,719)	$1,843	($6,392)	<0.001	*
Other	$659	($4,512)	$134	($2,129)	<0.001	*
Prescription drug	$3,151	($5,698)	$756	($3,310)	<0.001	*

Supplementary eTable 3. Comparison of MDD patients and controls in administrative claims data before patient matching, 2010[a]

Characteristics	MDD patients (N=50,197)		Controls (N=1,411,443)		P-value[b]	
MDD costs,[f] mean (SD)	$2,586	($7,387)	$0	($0)	<0.001	*
Medical service costs	$1,584	($7,047)	$0	($0)	<0.001	*
Inpatient	$557	($5,856)	$0	($0)	<0.001	*
Emergency department	$16	($273)	$0	($0)	<0.001	*
Outpatient	$887	($2,434)	$0	($0)	<0.001	*
Other	$124	($2,345)	$0	($0)	<0.001	*
Prescription drug	$1,002	($1,868)	$0	($0)	<0.001	*
GPI 58 (Antidepressants)	$597	($983)	$0	($0)	<0.001	*
GPI 59 (Antipsychotics/Antimanic Agents)	$405	($1,421)	$0	($0)	<0.001	*
Other depression costs,[f] mean (SD)	$781	($6,289)	$25	($408)	<0.001	*
Medical service costs	$606	($6,241)	$13	($315)	<0.001	*
Inpatient	$275	($5,938)	$2	($216)	<0.001	*
Emergency department	$40	($404)	$0	($36)	<0.001	*
Outpatient	$239	($1,035)	$10	($193)	<0.001	*
Other	$52	($908)	$0	($91)	<0.001	*
Prescription drug	$175	($652)	$13	($258)	<0.001	*
GPI 57 (Antianxiety Agents)	$28	($161)	$1	($27)	<0.001	*
GPI 72 (Anticonvulsants)	$147	($621)	$12	($257)	<0.001	*
Non-depression costs,[f] mean (SD)	$10,517	($46,436)	$3,887	($13,253)	<0.001	*
Mental health disorders	$877	($12,241)	$60	($1,133)	<0.001	*
Outpatient	$254	($1,647)	$24	($365)	<0.001	*
Inpatient	$412	($11,722)	$25	($976)	<0.001	*
Emergency department	$68	($766)	$7	($153)	<0.001	*
Rehab	$99	($1,804)	$2	($201)	<0.001	*
Other	$44	($613)	$2	($292)	<0.001	*
Non-mental health disorders	$7,667	($37,775)	$3,084	($12,331)	<0.001	*
Outpatient	$3,731	($12,855)	$1,809	($6,355)	<0.001	*
Inpatient	$3,199	($33,669)	$988	($9,012)	<0.001	*
Emergency department	$396	($1,834)	$157	($810)	<0.001	*
Rehab	$14	($324)	$6	($148)	<0.001	*
Other	$327	($2,918)	$124	($2,007)	<0.001	*
Prescription drug	$1,974	($4,944)	$743	($3,294)	<0.001	*
GPI 65 (Analgesics - Opioid)	$162	($1,489)	$10	($464)	<0.001	*
GPI 49 (Ulcer Drugs)	$129	($440)	$40	($231)	<0.001	*
GPI 60 (Hypnotics)	$61	($278)	$4	($58)	<0.001	*
GPI 61 (Adhd/Anti-Narcolepsy/Anti-Obesity/Anorexiants)	$181	($886)	$10	($179)	<0.001	*
Other non-depression related prescription drugs	$1,441	($4,309)	$679	($3,216)	<0.001	*
Workloss data						
	(N=10,576)		**(N=464,067)**			
Days of missed work, mean (SD)						
Total missed days	23.05	(46.41)	5.25	(16.74)	<0.001	*
Absenteeism days	11.46	(10.16)	3.76	(4.72)	<0.001	*
MDD absenteeism days	4.25	(5.53)	0.00	(0.00)	<0.001	*
Other depression absenteeism days	0.93	(3.12)	0.07	(0.84)	<0.001	*
Non-depression absenteeism days	6.28	(7.50)	3.70	(4.63)	<0.001	*
Disability days	11.59	(47.31)	1.49	(16.13)	<0.001	*
Costs of missed work, mean (SD)						
Total indirect costs	$4,296	($8,160)	$1,219	($2,823)	<0.001	*
Absenteeism costs	$3,297	($7,107)	$1,094	($2,449)	<0.001	*
MDD absenteeism costs	$1,256	($4,228)	$0	($0)	<0.001	*
Other depression absenteeism costs	$291	($1,501)	$27	($521)	<0.001	*
Non-depression absenteeism costs	$1,750	($4,524)	$1,067	($2,357)	<0.001	*
Disability costs	$1,000	($4,393)	$125	($1,366)	<0.001	*

Notes:

[a] Data source: OptumHealth Reporting and Insights[19,20].

[b] P-values were calculated using chi-squared tests for categorical variables and Wilcoxon rank sum tests for continuous variables. P-values <0.05 are indicated with an asterisk ("*").

[c] The 17 conditions included in the CCI were identified using ICD-9-CM diagnosis codes reported by Quan et al., 2005 [21] .

[d] Mental comorbidities were identified using ICD-9-CM diagnosis codes.

[e] Drugs were identified using the first two digits of the Generic Product Identifier (GPI).

[f] Costs reflect all costs paid for the service including patient out-of-pocket costs. Costs were inflated to 2012 USD using the medical care component of the Consumer Price Index.

Supplementary eTable 4. Comparison of MDD patients and controls in administrative claims data after patient matching, 2005[a]

Characteristics	MDD patients (N=33,375)		Controls (N=33,375)		P-value[b]	
Demographics						
Age, mean (SD)	43.9	(11.50)	43.9	(11.50)	1.000	
Gender, n (%) male	10,884	(32.6%)	10,884	(32.6%)	1.000	
Region, n (%)						
South	13,848	(41.5%)	13,848	(41.5%)	1.000	
Midwest	7,668	(23.0%)	7,668	(23.0%)	1.000	
West	4,825	(14.5%)	4,825	(14.5%)	1.000	
Northeast	6,955	(20.8%)	6,955	(20.8%)	1.000	
Other	79	(0.2%)	79	(0.2%)	1.000	
Insurance type, n (%)						
PPO	19,065	(57.1%)	19,065	(57.1%)	1.000	
POS	10,112	(30.3%)	10,112	(30.3%)	1.000	
Indemnity	2,921	(8.8%)	2,921	(8.8%)	1.000	
Other	1,277	(3.8%)	1,277	(3.8%)	1.000	
Employment status, n (%)						
Actively employed	25,512	(76.4%)	25,512	(76.4%)	1.000	
Retired	2,171	(6.5%)	2,389	(7.2%)	<0.001	*
Other	5,692	(17.1%)	5,474	(16.4%)	<0.001	*
Relationship to primary beneficiary, n (%)						
Self	19,536	(58.5%)	19,536	(58.5%)	1.000	
Spouse	11,633	(34.9%)	11,718	(35.1%)	<0.001	*
Child	2,118	(6.3%)	2,049	(6.1%)	<0.001	*
Other	88	(0.3%)	72	(0.2%)	0.197	
Charlson Comorbidity Index (CCI), mean (SD)[c]	0.33	(0.72)	0.33	(0.72)	1.000	
General physical comorbidities,[c] n (%)						
Hypertension	7,026	(21.1%)	6,885	(20.6%)	<0.001	*
Hypothyroidism	2,633	(7.9%)	2,623	(7.9%)	0.685	
Deficiency anemias	1,218	(3.6%)	1,212	(3.6%)	0.783	
Rheumatoid arthritis	629	(1.9%)	706	(2.1%)	<0.001	*
Neurological disorders	544	(1.6%)	535	(1.6%)	0.496	
Cardiac arrhythmias	694	(2.1%)	549	(1.6%)	<0.001	*
Valvular disease	640	(1.9%)	609	(1.8%)	0.151	
Fluid and electrolyte disorders	483	(1.4%)	485	(1.5%)	0.907	
Mental comorbidities,[d] n (%)						
Anxiety disorders	9,054	(27.1%)	515	(1.5%)	<0.001	*
Adjustment disorders	3,339	(10.0%)	467	(1.4%)	<0.001	*
Sleep disorders	2,953	(8.8%)	638	(1.9%)	<0.001	*
Mood disorders	3,103	(9.3%)	34	(0.1%)	<0.001	*
Miscellaneous other mental disorders	1,582	(4.7%)	240	(0.7%)	<0.001	*
ADD	1,278	(3.8%)	117	(0.4%)	<0.001	*
Alcohol abuse	1,233	(3.7%)	68	(0.2%)	<0.001	*
Screening for disorders	993	(3.0%)	323	(1.0%)	<0.001	*
Drug abuse	1,002	(3.0%)	41	(0.1%)	<0.001	*
Schizophrenia	733	(2.2%)	22	(0.1%)	<0.001	*
Sexual and gender identity disorders	846	(2.5%)	490	(1.5%)	<0.001	*
Drug use,[e] n (%)						
Antidepressants	26,665	(79.9%)	0	(0.0%)	1.000	
Antipsychotics	5,094	(15.3%)	0	(0.0%)	1.000	
Antimanics	763	(2.3%)	0	(0.0%)	1.000	
Medical resource use, mean (SD)						
Inpatient visits	0.32	(1.18)	0.09	(0.36)	<0.001	*
Inpatient days	1.27	(5.90)	0.34	(2.47)	<0.001	*
Rehab facility visits	0.06	(0.79)	0.00	(0.08)	<0.001	*
Rehab facility days	0.29	(3.52)	0.02	(0.70)	<0.001	*
Emergency department visits	0.64	(2.00)	0.28	(0.94)	<0.001	*
Outpatient visits	21.87	(16.95)	7.69	(8.98)	<0.001	*
Other visits	2.47	(5.67)	1.44	(3.34)	<0.001	*
Total direct costs,[f] mean (SD)	$9,648	($14,504)	$3,941	($9,405)	<0.001	*
Medical service costs	$6,707	($13,046)	$3,132	($8,893)	<0.001	*
Inpatient	$2,038	($9,243)	$968	($6,021)	<0.001	*
Emergency department	$333	($1,211)	$135	($714)	<0.001	*
Outpatient	$3,824	($6,099)	$1,867	($5,483)	<0.001	*
Other	$512	($3,343)	$163	($1,033)	<0.001	*
Prescription drug	$2,941	($4,524)	$809	($2,146)	<0.001	*

Supplementary eTable 4. Comparison of MDD patients and controls in administrative claims data after patient matching, 2005[a]

Characteristics	MDD patients (N=33,375)		Controls (N=33,375)		P-value[b]	
MDD costs,[f] mean (SD)	$2,294	($4,357)	$0	($)	<0.001	*
Medical service costs	$1,264	($3,891)	$0	($0)	<0.001	*
Inpatient	$387	($2,846)	$0	($0)	<0.001	*
Emergency department	$8	($134)	$0	($0)	<0.001	*
Outpatient	$773	($1,689)	$0	($0)	<0.001	*
Other	$96	($1,422)	$0	($0)	<0.001	*
Prescription drug	$1,030	($1,538)	$0	($0)	<0.001	*
GPI 58 (Antidepressants)	$783	($966)	$0	($0)	<0.001	*
GPI 59 (Antipsychotics/Antimanic Agents)	$248	($1,044)	$0	($0)	<0.001	*
Other depression costs,[f] mean (SD)	$675	($2,426)	$30	($374)	<0.001	*
Medical service costs	$412	($2,224)	$12	($283)	<0.001	*
Inpatient	$159	($1,744)	$1	($204)	<0.001	*
Emergency department	$22	($276)	$0	($34)	<0.001	*
Outpatient	$197	($872)	$10	($181)	<0.001	*
Other	$35	($619)	$0	($29)	<0.001	*
Prescription drug	$263	($806)	$18	($244)	<0.001	*
GPI 57 (Antianxiety Agents)	$49	($247)	$1	($19)	<0.001	*
GPI 72 (Anticonvulsants)	$214	($749)	$16	($244)	<0.001	*
Non-depression costs,[f] mean (SD)	$6,679	($12,749)	$3,911	($9,387)	<0.001	*
Mental health disorders	$436	($3,071)	$37	($651)	<0.001	*
Outpatient	$140	($744)	$17	($287)	<0.001	*
Inpatient	$171	($2,412)	$15	($565)	<0.001	*
Emergency department	$32	($319)	$3	($106)	<0.001	*
Rehab	$67	($1,039)	$0	($27)	<0.001	*
Other	$25	($653)	$1	($31)	<0.001	*
Non-mental health disorders	$4,595	($11,082)	$3,083	($8,824)	<0.001	*
Outpatient	$2,714	($5,496)	$1,839	($5,457)	<0.001	*
Inpatient	$1,322	($7,831)	$951	($5,961)	<0.001	*
Emergency department	$271	($1,059)	$131	($702)	<0.001	*
Rehab	$3	($113)	$3	($137)	0.010	*
Other	$285	($2,572)	$159	($1,001)	<0.001	*
Prescription drug	$1,647	($3,677)	$792	($2,124)	<0.001	*
GPI 65 (Analgesics - Opioid)	$151	($1,731)	$7	($148)	<0.001	*
GPI 49 (Ulcer Drugs)	$169	($478)	$62	($278)	<0.001	*
GPI 60 (Hypnotics)	$87	($272)	$4	($47)	<0.001	*
GPI 61 (Adhd/Anti-Narcolepsy/Anti-Obesity/Anorexiants)	$119	($531)	$4	($84)	<0.001	*
Other non-depression related prescription drugs	$1,121	($2,827)	$714	($2,052)	<0.001	*
Workloss data						
	(N=8,933)		**(N=8,933)**			
Days of missed work, mean (SD)						
Total missed days	21.42	(45.63)	5.23	(13.70)	<0.001	*
Absenteeism days	11.44	(9.63)	4.26	(4.69)	<0.001	*
MDD absenteeism days	4.26	(5.04)	0.00	(0.00)	<0.001	*
Other depression absenteeism days	1.03	(3.01)	0.07	(0.79)	<0.001	*
Non-depression absenteeism days	6.16	(7.09)	4.18	(4.61)	<0.001	*
Disability days	9.98	(46.70)	0.97	(12.96)	<0.001	*
Costs of missed work, mean (SD)						
Total indirect costs	$3,973	($6,044)	$1,263	($2,354)	<0.001	*
Absenteeism costs	$2,895	($3,242)	$1,157	($1,871)	<0.001	*
MDD absenteeism costs	$1,123	($1,890)	$0	($0)	<0.001	*
Other depression absenteeism costs	$271	($963)	$22	($318)	<0.001	*
Non-depression absenteeism costs	$1,502	($1,955)	$1,135	($1,808)	<0.001	*
Disability costs	$1,078	($5,559)	$106	($1,434)	<0.001	*

Notes:

[a] Data source: OptumHealth Reporting and Insights[19,20].

[b] P-values were calculated using chi-squared tests for categorical variables and Wilcoxon rank sum tests for continuous variables. P-values <0.05 are indicated with an asterisk ("*").

[c] The 17 conditions included in the CCI were identified using ICD-9-CM diagnosis codes reported by Quan et al. , 2005 [21].

[d] Mental comorbidities were identified using ICD-9-CM diagnosis codes.

[e] Drugs were identified using the first two digits of the Generic Product Identifier (GPI).

[f] Costs reflect all costs paid for the service including patient out-of-pocket costs. Costs were inflated to 2012 USD using the medical care component of the Consumer Price Index.

Supplementary eTable 5. Comparison of MDD patients and controls in administrative claims data after patient matching, 2010[a]

Characteristics	MDD patients (N=44,241)		Controls (N=44,241)		P-value[b]	
Demographics						
Age, mean (SD)	44.5	(12.23)	44.5	(12.23)	1.000	
Gender, n (%) male	15,380	(34.8%)	15,380	(34.8%)	1.000	
Region, n (%)						
South	11,230	(25.4%)	11,230	(25.4%)	1.000	
Midwest	11,452	(25.9%)	11,452	(25.9%)	1.000	
West	6,927	(15.7%)	6,927	(15.7%)	1.000	
Northeast	13,486	(30.5%)	13,486	(30.5%)	1.000	
Other	1,146	(2.6%)	1,146	(2.6%)	1.000	
Insurance type, n (%)						
PPO	30,037	(67.9%)	30,037	(67.9%)	1.000	
POS	8,482	(19.2%)	8,482	(19.2%)	1.000	
Indemnity	4,485	(10.1%)	4,485	(10.1%)	1.000	
Other	1,237	(2.8%)	1,237	(2.8%)	1.000	
Employment status, n (%)						
Actively employed	36,304	(82.1%)	36,304	(82.1%)	1.000	
Retired	3,370	(7.6%)	3,659	(8.3%)	<0.001	*
Other	4,567	(10.3%)	4,278	(9.7%)	<0.001	*
Relationship to primary beneficiary, n (%)						
Self	25,188	(56.9%)	25,188	(56.9%)	1.000	
Spouse	15,550	(35.1%)	15,669	(35.4%)	<0.001	*
Child	3,404	(7.7%)	3,307	(7.5%)	<0.001	*
Other	99	(0.2%)	77	(0.2%)	0.095	
Charlson Comorbidity Index (CCI), mean (SD)[c]	0.46	(1.10)	0.46	(1.10)	1.000	
General physical comorbidities,[c] n (%)						
Hypertension	10,193	(23.0%)	10,256	(23.2%)	0.102	
Hypothyroidism	4,071	(9.2%)	4,227	(9.6%)	<0.001	*
Deficiency anemias	2,425	(5.5%)	2,297	(5.2%)	<0.001	*
Rheumatoid arthritis	1,192	(2.7%)	1,142	(2.6%)	0.092	
Neurological disorders	1,338	(3.0%)	1,317	(3.0%)	0.112	
Cardiac arrhythmias	1,652	(3.7%)	1,230	(2.8%)	<0.001	*
Valvular disease	1,101	(2.5%)	835	(1.9%)	<0.001	*
Fluid and electrolyte disorders	1,002	(2.3%)	964	(2.2%)	0.161	
Mental comorbidities,[d] n (%)						
Anxiety disorders	16,205	(36.6%)	934	(2.1%)	<0.001	*
Adjustment disorders	6,466	(14.6%)	711	(1.6%)	<0.001	*
Sleep disorders	4,199	(9.5%)	773	(1.7%)	<0.001	*
Mood disorders	6,080	(13.7%)	103	(0.2%)	<0.001	*
Miscellaneous other mental disorders	2,965	(6.7%)	373	(0.8%)	<0.001	*
ADD	4,318	(9.8%)	245	(0.6%)	<0.001	*
Alcohol abuse	2,822	(6.4%)	176	(0.4%)	<0.001	*
Screening for disorders	1,775	(4.0%)	638	(1.4%)	<0.001	*
Drug abuse	2,414	(5.5%)	141	(0.3%)	<0.001	*
Schizophrenia	1,683	(3.8%)	48	(0.1%)	<0.001	*
Sexual and gender identity disorders	1,373	(3.1%)	666	(1.5%)	<0.001	*
Drug use,[e] n (%)						
Antidepressants	33,727	(76.2%)	0	(0.0%)	1.000	
Antipsychotics	7,696	(17.4%)	0	(0.0%)	1.000	
Antimanics	848	(1.9%)	0	(0.0%)	1.000	
Medical resource use, mean (SD)						
Inpatient visits	0.30	(1.12)	0.11	(0.48)	<0.001	*
Inpatient days	1.33	(6.08)	0.45	(2.94)	<0.001	*
Rehab facility visits	0.10	(0.96)	0.03	(0.48)	<0.001	*
Rehab facility days	0.51	(6.05)	0.05	(0.99)	<0.001	*
Emergency department visits	0.58	(1.71)	0.32	(1.02)	<0.001	*
Outpatient visits	23.12	(18.22)	8.37	(9.51)	<0.001	*
Other visits	2.11	(4.69)	1.14	(2.66)	<0.001	*
Total direct costs,[f] mean (SD)	$10,379	($20,450)	$4,391	($11,596)	<0.001	*
Medical service costs	$7,604	($19,144)	$3,465	($10,786)	<0.001	*
Inpatient	$2,305	($13,935)	$1,093	($7,541)	<0.001	*
Emergency department	$415	($1,631)	$178	($877)	<0.001	*
Outpatient	$4,359	($9,810)	$2,051	($5,998)	<0.001	*
Other	$524	($3,696)	$143	($1,511)	<0.001	*
Prescription drug	$2,776	($4,985)	$926	($3,288)	<0.001	*

Supplementary eTable 5. Comparison of MDD patients and controls in administrative claims data after patient matching, 2010[a]

Characteristics	MDD patients (N=44,241)		Controls (N=44,241)		P-value[b]	
MDD costs,[f] mean (SD)	$2,366	($5,611)	$0	($0)	<0.001	*
Medical service costs	$1,410	($5,184)	$0	($0)	<0.001	*
Inpatient	$411	($3,574)	$0	($0)	<0.001	*
Emergency department	$14	($227)	$0	($0)	<0.001	*
Outpatient	$865	($2,057)	$0	($0)	<0.001	*
Other	$121	($2,461)	$0	($0)	<0.001	*
Prescription drug	$955	($1,791)	$0	($0)	<0.001	*
GPI 58 (Antidepressants)	$584	($969)	$0	($0)	<0.001	*
GPI 59 (Antipsychotics/Antimanic Agents)	$371	($1,342)	$0	($0)	<0.001	*
Other depression costs,[f] mean (SD)	$620	($2,737)	$35	($483)	<0.001	*
Medical service costs	$470	($2,652)	$14	($386)	<0.001	*
Inpatient	$160	($2,065)	$4	($359)	<0.001	*
Emergency department	$35	($317)	$1	($36)	<0.001	*
Outpatient[7]	$231	($919)	$9	($131)	<0.001	*
General practitioners	$25	($108)	$1	($32)	<0.001	*
Mental health specialists	$86	($440)	$4	($87)	<0.001	*
Other outpatient	$120	($727)	$4	($81)	<0.001	*
Other	$44	($856)	$0	($21)	<0.001	*
Prescription drug	$150	($572)	$21	($291)	<0.001	*
GPI 57 (Antianxiety Agents)	$25	($151)	$1	($34)	<0.001	*
GPI 72 (Anticonvulsants)	$124	($543)	$20	($288)	<0.001	*
Non-depression costs,[f] mean (SD)	$7,394	($18,372)	$4,356	($11,509)	<0.001	*
Mental health disorders	$594	($4,121)	$70	($1,382)	<0.001	*
Outpatient	$234	($1,518)	$25	($341)	<0.001	*
Inpatient	$183	($2,759)	$37	($1,315)	<0.001	*
Emergency department	$51	($487)	$7	($131)	<0.001	*
Rehab	$89	($1,756)	$1	($70)	<0.001	*
Other	$37	($543)	$1	($24)	<0.001	*
Non-mental health disorders	$5,130	($16,170)	$3,382	($10,426)	<0.001	*
Outpatient	$3,029	($9,073)	$2,017	($5,955)	<0.001	*
Inpatient	$1,552	($11,683)	$1,053	($7,093)	<0.001	*
Emergency department	$316	($1,338)	$171	($853)	<0.001	*
Rehab	$10	($294)	$6	($129)	0.017	*
Other	$223	($1,436)	$135	($1,487)	<0.001	*
Prescription drug	$1,671	($4,227)	$904	($3,268)	<0.001	*
GPI 65 (Analgesics - Opioid)	$137	($1,449)	$13	($416)	<0.001	*
GPI 49 (Ulcer Drugs)	$115	($412)	$45	($246)	<0.001	*
GPI 60 (Hypnotics)	$57	($269)	$4	($56)	<0.001	*
GPI 61 (Adhd/Anti-Narcolepsy/Anti-Obesity/Anorexiants)	$171	($840)	$9	($191)	<0.001	*
Other non-depression related prescription drugs	$1,189	($3,581)	$833	($3,194)	<0.001	*
Workloss data						
	(N=9,990)		(N=9,990)			
Days of missed work, mean (SD)						
Total missed days	21.17	(42.84)	6.20	(20.03)	<0.001	*
Absenteeism days	11.19	(9.77)	4.15	(4.72)	<0.001	*
MDD absenteeism days	4.25	(5.40)	0.00	(0.00)	<0.001	*
Other depression absenteeism days	0.93	(3.16)	0.08	(0.83)	<0.001	*
Non-depression absenteeism days	6.00	(7.12)	4.08	(4.60)	<0.001	*
Disability days	9.98	(43.49)	2.05	(19.67)	<0.001	*
Costs of missed work, mean (SD)						
Total indirect costs	$4,084	($7,395)	$1,353	($2,882)	<0.001	*
Absenteeism costs	$3,219	($6,587)	$1,191	($2,391)	<0.001	*
MDD absenteeism costs	$1,265	($4,304)	$0	($0)	<0.001	*
Other depression absenteeism costs	$292	($1,519)	$28	($436)	<0.001	*
Non-depression absenteeism costs	$1,662	($3,587)	$1,163	($2,315)	<0.001	*
Disability costs	$865	($3,801)	$161	($1,621)	<0.001	*

Notes:

[a] Data source: OptumHealth Reporting and Insights[19,20].

[b] P-values were calculated using chi-squared tests for categorical variables and Wilcoxon rank sum tests for continuous variables. P-values <0.05 are indicated with an asterisk ("*").

[c] The 17 conditions included in the CCI were identified using ICD-9-CM diagnosis codes reported by Quan et al., 2005 [21].

[d] Mental comorbidities were identified using ICD-9-CM diagnosis codes.

[e] Drugs were identified using the first two digits of the Generic Product Identifier (GPI).

[f] Costs reflect all costs paid for the service including patient out-of-pocket costs. Costs were inflated to 2012 USD using the medical care component of the Consumer Price Index.

Supplementary eTable 6. Calculation of ratios used to infer missing cost categories

Cost category	MDD population employment/treatment status	Source	Ratio	Calculation	
Direct costs	Not employed/ treated and not treated	Literature (Ivanova et al., 2011)	Ratio of Medicaid to privately insured annual costs for MDD patients	Direct costs per patient per year for Medicaid patients with MDD	$ 17,960 [a]
				Direct costs per patient per year for privately insured patients with MDD	$ 10,442 [a]
				Ratio	**1.7**
Absenteeism/ disability costs	Employed/ not treated	Survey data (NSDUH)	Ratio of untreated to treated incremental days missed for illness/injury	Incremental days missed per month by individuals with MDD, not treated	0.54 [b]
				Incremental days missed per month by individuals with MDD, treated	1.13 [b]
				Ratio	**0.48**
Presenteeism costs	Employed/ treated and not treated	Literature (Stewart et al., 2003)	Ratio of presenteeism to absenteeism incremental cost	Incremental presenteeism costs ($billion per year)	$ 26.56 [c]
				Incremental absenteeism costs ($billion per year)	$ 4.37 [c]
				Ratio	**6.1**

Notes:

[a] Table 5 (p. 321) in Ivanova et al., 2011 [26].

[b] Calculated as the difference between the average number of days missed for illness/injury by individuals with vs. without MDD from 2005 to 2010, based on the variable WORKDAYS (number of workdays missed for injury/illness) in NSDUH data.[13,14]

[c] Calculated as the difference between "Any Depression" and "Expected Total Cost in the Absence of Depression" presenteeism/absenteeism mean cost per year (presenteeism: $35.73b - $9.17b = $26.56b; absenteeism: $8.27b - $3.90b = $4.37b) reported in Table 4 (p. 3141) of Stewart et al., 2003 [7].

Supplementary eTable 7. Incremental direct costs of individuals with MDD by employment status, treatment status, and age group, 2005 and 2010

	Total								
	2005			2010			Change		
	No. of Cases	Annual Cost per Case ($)	Total ($m)	No. of Cases	Annual Cost per Case ($)	Total ($m)	No. of Cases	Cost per Case	Total Cost
Total	**13,798,399**	**$5,618**	**$77,517**	**15,446,771**	**$6,400**	**$98,854**	11.9%	13.9%	27.5%
Employed	8,494,171	$4,060	$34,483	8,545,749	$4,521	$38,636	0.6%	11.4%	12.0%
Treated	3,934,227	$5,374	$21,144	4,372,366	$5,719	$25,005	11.1%	6.4%	18.3%
18-25	734,326	$4,693	$3,446	670,092	$5,667	$3,797	-8.7%	20.8%	10.2%
26-34	782,668	$3,869	$3,028	1,009,520	$4,207	$4,247	29.0%	8.7%	40.3%
35-49	1,608,748	$5,888	$9,472	1,519,257	$5,970	$9,070	-5.6%	1.4%	-4.2%
50+	808,485	$6,430	$5,199	1,173,497	$6,724	$7,890	45.1%	4.6%	51.8%
Not treated	4,559,944	$2,925	$13,338	4,173,383	$3,266	$13,631	-8.5%	11.7%	2.2%
18-25	1,243,755	$2,464	$3,064	1,082,350	$3,075	$3,328	-13.0%	24.8%	8.6%
26-34	1,026,313	$1,857	$1,906	817,331	$2,231	$1,824	-20.4%	20.1%	-4.3%
35-49	1,409,259	$3,474	$4,896	1,365,536	$3,426	$4,678	-3.1%	-1.4%	-4.5%
50+	880,617	$3,943	$3,472	908,166	$4,186	$3,802	3.1%	6.2%	9.5%
Not employed	5,304,228	$8,113	$43,034	6,901,021	$8,726	$60,218	30.1%	7.6%	39.9%
Treated	3,273,266	$9,741	$31,886	4,310,542	$10,404	$44,846	31.7%	6.8%	40.6%
18-25	369,467	$7,976	$2,947	450,910	$9,518	$4,292	22.0%	19.3%	45.6%
26-34	421,078	$6,553	$2,760	427,741	$7,126	$3,048	1.6%	8.7%	10.5%
35-49	1,225,959	$9,934	$12,179	1,221,636	$9,941	$12,144	-0.4%	0.1%	-0.3%
50+	1,256,761	$11,140	$14,000	2,210,256	$11,475	$25,363	75.9%	3.0%	81.2%
Not treated	2,030,962	$5,489	$11,149	2,590,480	$5,934	$15,371	27.5%	8.1%	37.9%
18-25	479,996	$4,232	$2,031	617,783	$5,159	$3,187	28.7%	21.9%	56.9%
26-34	329,180	$3,325	$1,095	322,393	$3,847	$1,240	-2.1%	15.7%	13.3%
35-49	538,823	$6,076	$3,274	598,263	$5,997	$3,588	11.0%	-1.3%	9.6%
50+	682,963	$6,953	$4,749	1,052,041	$6,992	$7,356	54.0%	0.6%	54.9%

Supplementary eTable 8. ICD-9-CM codes accounting for at least 1% of the incremental cost per patient for non-mental health medical services[a] in 2010 (in 2012 dollars)

ICD-9-CM	ICD-9-CM description	Cost per patient with MDD	Cost per patient w/o MDD	Incremental cost per patient	% of total incremental cost
722	Intervertebral disc disorders	$233	$69	$164	9.4%
724	Other and unspecified disorders of back (e.g., lumbago)	$159	$56	$103	5.9%
789	Other symptoms involving abdomen and pelvis (e.g., abdominal pain)	$124	$57	$67	3.9%
786	Symptoms involving respiratory system and other chest symptoms (e.g., chest pain)	$145	$81	$64	3.7%
723	Other disorders of cervical region (e.g., cervicalgia)	$83	$28	$55	3.2%
780	General symptoms (e.g., sleep disturbances, malaise and fatigue)	$97	$47	$50	2.9%
721	Spondylosis and allied disorders	$68	$21	$47	2.7%
327	Organic sleep disorders	$68	$22	$46	2.7%
278	Overweight, obesity and other hyperalimentation	$62	$31	$31	1.8%
996	Complications peculiar to certain specified procedures	$57	$27	$29	1.7%
719	Other and unspecified disorders of joint	$75	$46	$29	1.7%
726	Peripheral enthesopathies and allied syndromes	$63	$34	$29	1.6%
V58	Encounter for other and unspecified procedures and aftercare	$65	$36	$28	1.6%
784	Symptoms involving head and neck (e.g., headache)	$46	$18	$28	1.6%
787	Symptoms involving digestive system	$44	$18	$26	1.5%
998	Other complications of procedures, NEC	$32	$9	$23	1.3%
729	Other disorders of soft tissues (e.g., rheumatism, myalgia and myositis)	$40	$19	$21	1.2%
530	Diseases of esophagus	$37	$16	$21	1.2%
279	Disorders involving the immune mechanism	$23	$3	$20	1.2%
346	Migraine	$24	$4	$20	1.1%
715	Osteoarthrosis and allied disorders	$137	$119	$18	1.1%
473	Chronic sinusitis	$29	$11	$17	1.0%
592	Calculus of kidney and ureter	$50	$33	$17	1.0%
625	Pain and other symptoms associated with female genital organs	$32	$15	$17	1.0%
738	Other acquired deformity	$20	$4	$17	1.0%
338	Pain, not elsewhere classified	$20	$4	$16	0.9%
All other diagnosis codes		$3,295	$2,550	$744	42.6%
Total		**$5,130**	**$3,382**	**$1,748**	**100.0%**

[a] Data source: OptumHealth Reporting and Insights[19,20].

Supplementary eTable 9. Number of suicides and loss of lifetime earnings due to MDD, 2005 and 2010[a]

2005

	Total number of suicides		Number of suicides related to MDD		Present value of lifetime earnings[b] (discounted at 3%)		Total earnings lost (in millions) (discounted at 3%)	
	Male	Female	Male	Female	Male	Female	Male	Female
Age (y)	**[A]**	**[B]**	**[C] = [A] x 0.5**	**[D] = [B] x 0.5**	**[E]**	**[F]**	**[G] = [C] x [E]**	**[H] = [D] x [F]**
18-24	2,930	535	1,465	268	$1,082,414	$675,240	$1,586	$181
25-29	1,975	402	988	201	$1,127,178	$686,021	$1,113	$138
30-34	2,091	522	1,046	261	$1,080,431	$645,539	$1,130	$168
35-39	2,259	634	1,130	317	$981,758	$585,127	$1,109	$185
40-44	2,804	853	1,402	427	$840,666	$505,952	$1,179	$216
45-49	2,826	938	1,413	469	$677,117	$410,952	$957	$193
50-54	2,443	784	1,222	392	$501,391	$297,106	$612	$116
55-59	1,888	589	944	295	$318,111	$177,603	$300	$52
60-64	1,362	371	681	186	$158,315	$79,574	$108	$15
65+	4,550	854	2,275	427	$31,688	$12,019	$72	$5
Total	25,128	6,482	12,564	3,241			$8,165	$1,270
Mortality costs								**$9,435**

2010

	Total number of suicides		Number of suicides related to MDD		Present value of lifetime earnings[b] (discounted at 3%)		Total earnings lost (in millions) (discounted at 3%)	
	Male	Female	Male	Female	Male	Female	Male	Female
Age (y)	**[A]**	**[B]**	**[C] = [A] x 0.5**	**[D] = [B] x 0.5**	**[E]**	**[F]**	**[G] = [C] x [E]**	**[H] = [D] x [F]**
18-24	3,213	652	1,607	326	$931,237	$622,439	$1,496	$203
25-29	2,459	541	1,230	271	$982,404	$639,317	$1,208	$173
30-34	2,184	551	1,092	276	$952,597	$607,087	$1,040	$167
35-39	2,372	712	1,186	356	$870,462	$550,716	$1,032	$196
40-44	2,661	826	1,331	413	$751,243	$479,929	$1,000	$198
45-49	3,375	997	1,688	499	$612,887	$392,283	$1,034	$196
50-54	3,358	1,069	1,679	535	$460,817	$293,880	$774	$157
55-59	2,859	901	1,430	451	$305,794	$186,749	$437	$84
60-64	2,010	614	1,005	307	$164,915	$91,378	$166	$28
65+	5,035	959	2,518	480	$37,610	$15,694	$95	$8
Total	29,526	7,822	14,763	3,911			$8,282	$1,410
Mortality costs								**$9,691**

Notes:

[a] Data sources: Centers for Disease Control and Prevention, 2014 [27], Kung et al., 2008 [31], Murphy et al. 2012 [32], U.S. Bureau of Labor Statistics, 2006 [33] and 2011 [34].

[b] Lifetime earnings are expressed in 2012 dollars.

Supplementary eTable 10. Incremental workplace costs of individuals with MDD, 2005 and 2010 (in 2012 dollars)

Cost category	2005 Incremental missed days per individual	2005 Incremental cost per individual	2010 Incremental missed days per individual	2010 Incremental cost per individual
MDD costs				
Absenteeism	2.6	$1,483	2.9	$1,680
Disability	2.5	$628	2.5	$439
Presenteeism[a]	12.0	$6,849	13.3	$7,715
Other depression costs				
Absenteeism	1.6	$466	1.5	$466
Disability	1.3	$165	1.1	$104
Presenteeism[a]	6.3	$1,801	5.8	$1,820
Non-depression costs				
Absenteeism	3.4	$684	3.3	$881
Disability	2.7	$243	2.4	$196
Presenteeism[a]	13.1	$2,647	12.9	$3,438
Total				
Absenteeism	7.6	$1,837	7.7	$2,206
Disability	6.5	$699	5.9	$524
Presenteeism[a]	31.5	$7,621	31.9	$9,206
Total incremental cost per individual [A]		**$10,156**		**$11,936**
Total number of MDD employed individuals [B]		**8,494,171**		**8,545,749**
Societal workplace cost (in millions) [C]=[A]*[B]		**$86,268**		**$102,003**

[a] Presenteeism costs are expressed here in terms of full-work day equivalents missed. These estimates were derived using the same cost per day underlying absenteeism calculations.