

Research paper

The economic burden of bipolar I disorder in the United States in 2015

Martin Cloutier^a, Mallik Greene^{b,*}, Annie Guerin^a, Maelys Touya^c, Eric Wu^d^a Analysis Group, Inc., Montreal, Quebec, Canada^b Health Economics & Outcomes Research, Otsuka Pharmaceutical Development & Commercialization, Inc., Princeton, NJ, USA^c Health Economics and Outcomes Research (HEOR)-US, Lundbeck, Deerfield, IL, USA^d Analysis Group, Inc., Boston, MA, USA

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ABSTRACT

Background: The current societal costs of bipolar I disorder (BDI) have not been comprehensively characterized in the United States, as previous studies are based on data from two decades ago.

Methods: The costs of BDI were estimated for 2015 and comprised direct healthcare costs, non-healthcare costs, and indirect costs, calculated based on a BDI prevalence of 1%. The excess costs of BDI were estimated as the difference between the costs incurred by individuals with BDI and those incurred by individuals without BD or individuals from the general population. Direct healthcare costs were assessed using three large US claims databases for insured individuals and the literature for uninsured individuals. Direct non-healthcare and indirect costs were based on the literature and governmental publications.

Results: The total costs of BDI were estimated at \$202.1 billion in 2015, corresponding to an average of \$81,559 per individual, while the excess costs of BDI were estimated at \$119.8 billion, corresponding to an average of \$48,333 per individual. The largest contributors to excess costs were caregiving (36%), direct healthcare costs (21%), and unemployment (20%). In sensitivity analyses, excess costs ranged from \$101.2 to \$124.3 billion.

Limitations: Direct healthcare costs were calculated based on a BDI diagnosis, thus excluding undiagnosed patients. Direct non-healthcare and indirect costs were based on combined estimates from the literature.

Conclusions: Besides direct healthcare costs, BDI was associated with substantial direct non-healthcare and indirect costs. More effective treatments and practices are needed to optimize therapeutic strategies and contain direct and indirect costs.

1. Introduction

Bipolar disorder (BD) is a chronic mental disorder characterized by manic, hypomanic, and major depressive episodes (Anderson et al., 2012). The most recent version of the American Psychiatric Association (APA) Diagnostic and Statistical Manual of Mental Disorders (DSM) classifies BD into four main subtypes (American Psychiatric Association, 2013): Bipolar I disorder (BDI), bipolar II disorder (BDII), cyclothymia, and BD not otherwise specified. Collectively, the four BD subtypes are estimated to affect 4.4% of the population in the United States (US), with BDI and BDII each associated with a prevalence of approximately 1% (Merikangas et al., 2007b, 2011).

BDI is typically the most severe form of BD (Escamilla and Zavala, 2008). Symptoms of BDI include hyperactivity, decreased need for sleep, pressured speech, irritability, agitation, and altered judgment (Belmaker, 2004; National Institute of Mental Health, 2016). The sudden changes in mood and behavior that characterize BDI adversely affect many aspects of the lives of both patients and caregivers

including employment, financial functioning, and social interactions (Hawke et al., 2013; IsHak et al., 2012; Michalak et al., 2007). Compared to the general population, individuals with BDI are known to present a higher suicide rate and an increased number of comorbidities such as respiratory diseases, diabetes, cardiovascular diseases, human immunodeficiency virus, and hepatitis C (Carney and Jones, 2006; Crump et al., 2013). Altogether, individuals with BDI incur substantial direct healthcare costs (e.g. medical and pharmaceutical costs), direct non-healthcare costs (e.g. substance abuse-related costs), and indirect costs (e.g. costs associated with reduced productivity, unemployment, and caregiving) (Kleinman et al., 2003; Wyatt and Henter, 1995).

Nevertheless, the current costs of BDI have not been comprehensively characterized in the US from a societal perspective. To the best of our knowledge, the few existing estimates of the societal costs of BD are based on data from the 1990's or mostly focus on a limited number of cost components (Begley et al., 2001; Wyatt and Henter, 1995). Given that, over the past two decades, the management of BDI and mental health policies and coverage have undergone several changes in the US

* Correspondence to: Health Economics and Outcomes Research, Otsuka Pharmaceutical Development & Commercialization, Inc., Princeton, NJ, USA
E-mail address: mallik.greene@otsuka-us.com (M. Greene).

(Gitlin and Frye, 2012; Harrison et al., 2016; McGinty et al., 2015; Park et al., 2008), these estimates are likely to be outdated. Contemporary estimates of the societal costs of BDI are needed to provide healthcare stakeholders with updated information that may help optimize decision making and resource allocation. Accordingly, this study aimed to address the following research question: what are the total and excess costs associated with BDI from a societal perspective in the US.

2. Methods

2.1. Economic burden estimate

The economic burden of BDI was estimated for the year 2015 (the most recent year available in the data to estimate direct healthcare costs) and comprised direct healthcare costs, direct non-healthcare costs, and indirect costs.

Costs associated with BDI were calculated using a prevalence-based approach considering a BDI prevalence of 1.0% and the 2015 Census Bureau estimate of the US adult population (Merikangas et al., 2007a; US Census Bureau, 2015). As part of this approach, the total costs were first estimated based on the costs incurred by individuals with BDI. Successively, to estimate the incremental burden associated with BDI, the excess costs of BDI were estimated as the difference between the costs incurred by individuals with BDI (or with BD when BDI-specific cost estimates were not available) and those incurred by individuals from the general population, depending on the information available for each cost component. In the event a cost associated with a component was by definition an excess cost, total costs for individuals with BDI were defined as the excess costs of BDI and total costs of the general population were set to zero.

All costs were expressed in 2015 US dollars. Direct healthcare costs were adjusted to 2015 US dollars using the Consumer Price Index for All Urban Consumers (CPI-U), Medical Care (US Bureau of Labor Statistics, 2017a), while direct non-healthcare costs and indirect costs were adjusted using the CPI-U, All Items (US Bureau of Labor Statistics, 2017a).

All the data used in this study were compliant with the Health Insurance Portability and Accountability Act and did not contain identifiable patient information; no institutional review board approval was necessary. For all components, when information was available from multiple data sources, data from governmental publications were prioritized. When not available, other sources were considered based on the relevance and representativeness of the data. Weighted average techniques were used to incorporate information from several data sources when appropriate. The data sources used to estimate the different types of costs are detailed in the sections below.

2.1.1. Direct healthcare costs

Direct healthcare costs were estimated using a retrospective matched cohort design. They included medical and pharmacy costs and were assessed separately for insured (commercial, Medicare, and Medicaid coverage) and uninsured individuals.

2.1.1.1. Insured individuals. For the analysis of the costs incurred by insured individuals, data were derived from three large administrative US claims databases: Truven Health Analytics MarketScan® Commercial Claims and Encounters, Truven Health Analytics MarketScan® Medicare Supplemental, and Truven Health Analytics MarketScan® Medicaid Multi-State. These databases include healthcare plan enrollment history and claims for medical (provider and institutional) and pharmacy services of enrollees and their dependents. For all three databases, the data covered the period from January 2010 to December 2015.

Two cohorts were defined: the *BDI cohort* and the *non-BD cohort*. The BDI cohort comprised all adult patients (i.e. at least 18 years old) from the Truven Health Analytics MarketScan® databases with at least one diagnosis of BDI (based on International Classification of Diseases, 9th

and 10th Revision codes, i.e. ICD-9 and ICD-10 codes) and at least 12 months of continuous health plan coverage following a diagnosis of BDI, including at least one month in 2015. The non-BD cohort comprised all adult patients (i.e. at least 18 years old) from the Truven Health Analytics MarketScan® databases without a documented diagnosis of any type of BD (based on ICD-9 and ICD-10 codes) during the entire period covered by the data and with at least 12 months of continuous health plan coverage, including at least one month in 2015. All types of BD were excluded from this control cohort to avoid selecting patients with a potential misdiagnosis of BDI. For both cohorts, Medicare-insured patients were at least 65 years of age as of the index date (defined as the last calendar date preceding 12 months of continuous health plan coverage), while commercially and Medicaid-insured patients were under 65 years of age until the end of the study period, defined as the 12-month period following the index date.

Patients with BDI were matched on up to a 1:3 ratio to non-BD patients having the same age, gender, region of residence (commercial and Medicare only), race (Medicaid only), health plan type, and the year of the index date.

For the BDI cohort, for each type of coverage, demographic characteristics were summarized and direct healthcare costs estimated based on the sum of the amounts reimbursed by payers and patients' out-of-pocket costs.

2.1.1.2. Uninsured individuals. For uninsured individuals, direct healthcare costs were estimated based on the average medical costs reported in the literature for the general uninsured population (Coughlin et al., 2014) and the ratio of the direct healthcare costs of the BDI cohort to those of the non-BD cohort, as measured in the analysis of insured individuals.

2.1.2. Direct non-healthcare costs

Direct non-healthcare costs included research on BDI as well as substance abuse-related expenditures. Their estimates were based on the most recent literature and governmental publications. In particular, the costs of research were drawn directly from the estimates of funding for research on BDI reported by the National Institute of Health (US Department of Health and Human Services National Institute of Health, 2016). Substance abuse-related costs included costs associated with the criminal justice system, property and personal costs incurred by victims of crimes, costs associated with loss of productivity for incarcerated individuals, prevention and research costs, and costs associated with motor vehicle accidents (for alcohol abuse only – based on availability) (Bouchery et al., 2011; Collins and Lapsley, 2008; US Department of Justice, 2011). For individuals with BDI, these costs were estimated based on the average substance abuse-related costs per individual reported in the US and the rate of substance abuse among individuals with BDI compared to that of the US general population, in the case of alcohol, drug, and alcohol/drug abuse disorders (Kessler et al., 2005a).

2.1.3. Indirect costs

Indirect costs included costs associated with productivity loss from unemployment, reduced productivity at work, productivity loss from premature mortality (for all cause and suicide-related deaths), and caregiving costs (i.e. productivity loss from caregiving and incremental healthcare costs incurred by caregivers). These costs were based on the most recent literature and governmental publications and were estimated using the human capital approach. More specifically, costs associated with productivity loss from unemployment were estimated based on the employment-to-population ratio in the BDI population (Kupfer et al., 2002) and the US population (US Census Bureau, 2015), and the average annual wage in the US employed population (US Bureau of Labor Statistics, 2017b). Costs of reduced productivity at work were estimated based on the productivity weight in the BDI employed population compared to the US population (Kleinman et al., 2005), the employment to population ratio in the BDI population

(Kupfer et al., 2002), and the average annual wage in the US employed population (US Bureau of Labor Statistics, 2017b). Costs of productivity loss from premature all-cause mortality were estimated based on the all-cause excess mortality rate per age group in the BDI population compared to the US population (Kochanek et al., 2016; Westman et al., 2013), the average age of retirement in the US population (which was used to assess the number of years of productive life lost) (Munnell, 2015), and the average annual wage per age group (US Bureau of Labor Statistics, 2015) in the US employed population (US Bureau of Labor Statistics, 2017b). The cost of productivity loss from premature all-cause mortality was discounted at a 3% rate (Greenberg et al., 2015) to obtain the net present value of future costs. Costs of productivity loss from suicide were reported separately as a subcategory of all-cause mortality using the same approach with suicide rates instead of all-cause mortality rates (Kochanek et al., 2016; Westman et al., 2013).

Costs of caregiving were calculated as the sum of productivity loss from caregiving and incremental healthcare costs incurred by caregivers. Costs associated with productivity loss from caregiving were estimated based on the number of unpaid hours devoted by caregivers to individuals with BDI (National Alliance for Caregiving, 2016, 2015), the proportion of individuals with BDI living with their family (Kupfer et al., 2002), and the average hourly wage in the US (US Bureau of Labor Statistics, 2017b). Incremental healthcare costs incurred by caregivers were estimated based on the excess direct healthcare costs incurred by family members of individuals with BDI compared to the US general population (Gianfrancesco et al., 2005), the proportion of individuals with BDI living with their families (Kupfer et al., 2002), and the average family size of individuals with BDI (Gianfrancesco et al., 2005).

2.2. Sensitivity analysis

To assess the robustness of the cost estimates, four sensitivity analyses were conducted: (1) uninsured individuals with BDI were assumed to incur no excess direct healthcare costs compared to non-BDI individuals (Cloutier et al., 2016; Wu et al., 2005); (2) the average substance abuse-related costs per individual with both alcohol and drug abuse were assumed to be equal to the average substance abuse-related costs per individual with drug abuse only; (3) the net present value of future costs of productivity loss from premature mortality was calculated based on the discount rates of 0% and 5%; and (4) the number of hours devoted to caregiving was varied based on an estimate from a previous study (Janssen, 2012).

3. Results

Based on a prevalence of 1.0%, the total adult BDI population in the US in 2015 was estimated at 2,477,737 individuals. These individuals were associated with a 2015 total cost of \$202.1 billion, comprising direct healthcare costs, direct non-healthcare costs, and indirect costs (Table 1); this corresponds to an average cost of \$81,559 per individual with BDI. The largest contributors to this total cost were unemployment costs (36%), caregiving costs (25%), and direct healthcare costs (23%) (Fig. 1).

When compared to the costs incurred by the US general population, this represents an excess cost of \$119.8 billion for BDI and \$48,333 per individual with BDI (Table 1). The largest contributors to this excess cost were caregiving costs (36%), direct healthcare costs (21%), and unemployment costs (20%) (Fig. 1).

3.1. Direct healthcare costs

Direct healthcare costs were estimated based on 107,943 commercially insured, 9436 Medicare-insured, and 84,640 Medicaid-insured patients with BDI (Table 2) who, on average, incurred \$17,468, \$30,757, and \$20,764 direct healthcare costs, respectively (Fig. 2).

While absolute costs varied across the different types of coverage, the excess costs associated with BDI were consistent across all the types of coverage: the average excess cost per patient with BDI was \$10,718 for commercially insured patients, \$11,591 for Medicare-insured patients, and \$10,941 for Medicaid-insured patients (Fig. 2).

Medical costs for uninsured individuals were based on the annual average cost reported in the literature for uninsured individuals in the US (Coughlin et al., 2014) and amounted to \$2567 (Fig. 2). Because direct healthcare costs of BDI patients were roughly two times higher than those of patients without BD for all three types of coverage, a 2:1 ratio was applied and the cost of uninsured patients with BDI was estimated at \$5134.

These average excess costs per patient with BDI for each type of coverage translated to an excess direct healthcare cost of \$25.2 billion, which comprised excess costs for outpatient (\$7.5 billion), inpatient (\$7.4 billion), pharmacy (\$7.0 billion), emergency room (\$2.3 billion), long-term care (\$0.3 billion), and other medical services (\$0.1 billion) (Table 1).

3.2. Direct non-healthcare costs

Costs related to research on BDI were estimated by the National Institute of Mental Health at \$0.1 billion (US Department of Health and Human Services National Institute of Health, 2016).

Based on the substance abuse-related costs reported in the literature, the average costs per individual suffering from a substance abuse disorder in the US were estimated at \$1226 for individuals with an alcohol abuse disorder, \$6304 for those with a drug abuse disorder, and \$7530 for those with both alcohol and drug abuse disorders (Bouchery et al., 2011; Collins and Lapsley, 2008; US Department of Justice, 2011).

Given that the prevalence of substance abuse disorder in the BDI population (18.5% for alcohol only; 26.2% for drug only, and 55.4% for both alcohol and drug) (Cassidy et al., 2001) is higher than that in the US population (14.6% for any substance abuse disorder) (Kessler et al., 2005a), the excess substance abuse rate of 44.8% yielded a substance abuse-related excess cost of \$6.7 billion.

Altogether, these costs related to research on BDI and substance abuse-related costs translated into an excess direct non-healthcare cost of \$6.8 billion.

3.3. Indirect costs

The employment-to-population ratio of the BDI and the US populations were estimated at 38.5% (Kupfer et al., 2002) and 58.8% (US Census Bureau, 2015), respectively. This yielded a difference in the employment-to-population ratio of 20.3%. Based on the US average annual wage of \$48,320 (US Bureau of Labor Statistics, 2017b), the excess costs associated with productivity loss from unemployment were estimated at \$24.2 billion.

Among employed individuals with BDI, reduced work productivity was also reported, with a productivity weight of 79.9% compared to the US population (Kleinman et al., 2005). Based on an employment to population ratio in the BDI population of 38.6% (Kupfer et al., 2002), this reduced productivity at work translated to an excess cost of \$9.3 billion.

Substantial costs related to productivity loss were also associated with premature mortality. The annual all-cause mortality rate for the BDI population was estimated to be 3.4–11.4 times higher, depending on the age group, than for the US population (Kochanek et al., 2016; Westman et al., 2013). Suicide, which is a notable cause of premature mortality in the BDI population, was found to be 10.3–16.2 times more common among individuals with BDI (Kochanek et al., 2016; Westman et al., 2013). For both all-cause and suicide-related mortality rates, the largest differences between the BDI and the US populations were observed among the younger age groups. Based on these differences in

Table 1
Societal Costs Associated with Bipolar I Disorder in the United States in 2015.

| Component | Total BDI Population | Counterfactual US Population | Excess Costs of BDI |
|---|--------------------------|------------------------------|--------------------------|
| Direct Healthcare Costs | | | |
| Pharmacy Costs | \$11,516,602,726 | \$4,508,706,186 | \$7,007,896,540 |
| Total Medical Service Costs | \$33,796,539,363 | \$16,466,116,766 | \$17,330,422,597 |
| Outpatient | \$16,485,375,175 | \$8,963,206,836 | \$7,522,168,339 |
| Inpatient | \$13,329,078,124 | \$5,963,561,233 | \$7,365,516,892 |
| Emergency Room | \$3,629,276,008 | \$1,308,223,318 | \$2,321,052,690 |
| Other Medical Services | \$352,810,056 | \$231,125,379 | \$121,684,677 |
| Long-Term Care Costs | \$460,072,807 | \$184,976,789 | \$275,096,017 |
| Direct Healthcare Costs | \$46,905,357,393 | \$21,725,870,990 | \$25,179,486,403 |
| Direct Non-healthcare Costs | | | |
| Bipolar Disorder-related Research | \$83,000,000 | \$0 | \$83,000,000 |
| Substance Abuse | \$8,903,656,296 | \$2,187,013,121 | \$6,716,643,175 |
| Direct Non-healthcare Costs | \$8,986,656,296 | \$2,187,013,121 | \$6,799,643,175 |
| Indirect Costs | | | |
| Unemployment | \$73,570,555,428 | \$49,326,393,550 | \$24,244,161,878 |
| Productivity Loss | \$9,285,893,825 | \$0 | \$9,285,893,825 |
| Premature Mortality (All-cause) | \$12,624,015,055 | \$2,018,202,284 | \$10,605,812,770 |
| Premature Mortality (Suicide) | \$2,379,598,715 | \$160,324,754 | \$2,219,273,961 |
| Caregiving - Productivity Costs | \$49,822,796,639 | \$7,068,286,028 | \$42,754,510,611 |
| Caregiving - Direct Healthcare Costs To Caregivers | \$886,274,902 | \$0 | \$886,274,902 |
| Indirect Costs | \$146,189,535,849 | \$58,412,881,863 | \$87,776,653,986 |
| Direct Healthcare, Direct Non-healthcare, and Indirect Costs | \$202,081,549,538 | \$82,325,765,973 | \$119,755,783,565 |

Based on a prevalence of 1.0%, the adult US bipolar I disorder population was estimated at 2,477,737 individuals in 2015. Costs were adjusted to 2015 US dollars using the Consumer Price Index. Estimates for the counterfactual US population were obtained by multiplying the average costs per adult individual in the US population by the number of adult individuals with bipolar I disorder in the US.

mortality rates, the average US retirement age of 63 years (Munnell, 2015), average annual wage of \$20,826 to \$49,799 (US Bureau of Labor Statistics, 2017b; US Census Bureau, 2015), and employment to population ratios of 29.9–77.6% (US Census Bureau, 2015) depending on the age group, the excess costs associated with premature all-cause mortality were estimated at \$10.6 billion, \$2.2 billion of which were associated with suicide.

In terms of caregiving, studies have reported that, on average, 28.9 h per week are devoted to caregiving for each individual with BDI (National Alliance for Caregiving, 2016) compared to 4.1 h in the US general population (National Alliance for Caregiving, 2015), amounting to an excess of 24.8 h per week. Given that 57.6% of individuals with BDI live with family members (Kupfer et al., 2002) and the US average hourly wage is \$23 (US Bureau of Labor Statistics, 2017b), this loss of productivity related to caregiving translated to an excess cost of \$42.8 billion.

In addition to productivity loss, caregivers have also been associated

with incremental direct healthcare costs; an annual excess direct healthcare cost of \$417 per family member has been estimated by Gianfrancesco et al. (2005). Considering that, on average, 57.6% of individuals with BDI live with family members and the average number of family members is 1.49, this represents an excess cost of \$0.9 billion.

Overall, excess indirect costs amounted to \$87.8 billion when costs associated with productivity loss from unemployment, reduced productivity at work, and productivity loss related to premature mortality and caregiving as well as incremental direct healthcare costs were considered.

When varying the parameters for the direct healthcare costs incurred by uninsured individuals with BDI, the average substance abuse-related costs per individual for both alcohol and drug abuse, the discount rate to estimate the net present value of future costs of productivity loss from premature mortality, and the number of hours devoted to caregiving, the most and least conservative estimates of the total costs of BDI ranged from \$182.5 to \$207.3 billion and the excess

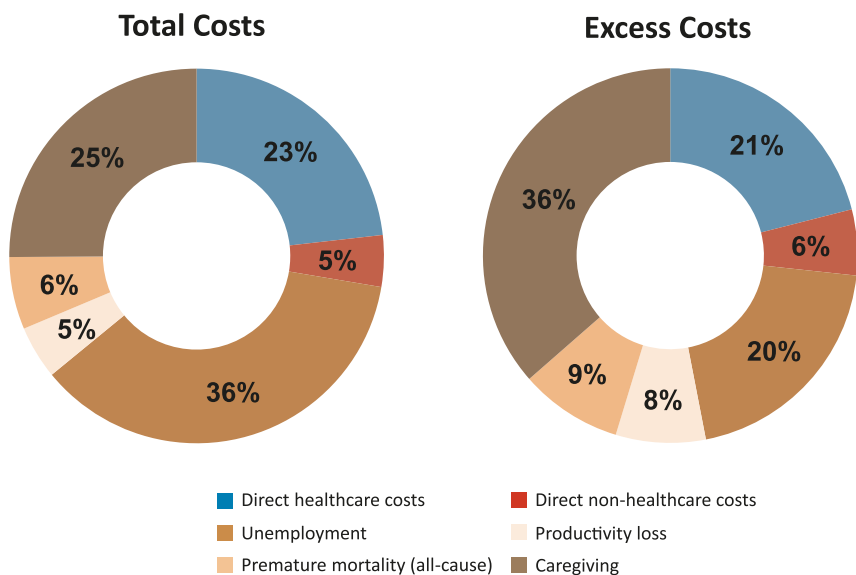


Fig. 1. Distribution of total and Excess Costs Associated with Bipolar I Disorder in the United States in 2015.

Table 2
Demographic characteristics of Insured Individuals with Bipolar I Disorder Costs.

| Patient Characteristics | Commercially Insured N = 107,943 | Medicare Insured N = 9436 | Medicaid Insured N = 84,640 |
|---|-------------------------------------|------------------------------|--------------------------------|
| Age, Mean ± SD [Median] | 41.6 ± 13.8 [43.5] | 75.3 ± 6.9[73.5] | 37.3 ± 12.4 [35.6] |
| Female, N (%) | 68,198 (63.2) | 5928 (62.8) | 60,045 (70.9) |
| Health Plan Type, N (%) | | | |
| Comprehensive | 4699 (4.4) | 4335 (45.9) | 56,960 (67.3) |
| Consumer Driven Health Plan | 12,188 (11.3) | 39 (0.4) | – |
| Exclusive Provider Organization | 994 (0.9) | 5 (0.1) | – |
| High Deductible Health Plan | 5656 (5.2) | 7 (0.1) | – |
| Home Maintenance Organization | 10,985 (10.2) | 862 (9.1) | 27,679 (32.7) |
| Point of Service, Partially or FullyCapitated | 612 (0.6) | 6 (0.1) | – |
| Point of Service, Uncapitated | 7186 (6.7) | 376 (4.0) | – |
| Preferred Provider Organization | 64,729 (60.0) | 3800 (40.3) | – |
| Unknown | 894 (0.8) | 6 (0.1) | 1 (0.0) |
| Region of Residence, N (%) | | | |
| North Central | 23,176 (21.5) | 3473 (36.8) | – |
| Northeast | 21,657 (20.1) | 2128 (22.6) | – |
| South | 45,151 (41.8) | 2816 (29.8) | – |
| West | 17,724 (16.4) | 1015 (10.8) | – |
| Unknown | 235 (0.2) | 4 (0.0) | – |
| Race, N (%) | | | |
| Black | – | – | 19,721 (23.3) |
| Hispanic | – | – | 1109 (1.3) |
| White | – | – | 52,118 (61.6) |
| Other | – | – | 11,692 (13.8) |

The symbol “–” indicates data not available. Patients were selected in the bipolar I disorder cohort if they had one documented diagnosis for bipolar I disorder: International Classification of Diseases, 9th Revision [ICD-9]/ICD-10 codes: 296.0x, 296.4x, 296.5x, 296.6x, 296.7x/F31.0, F31.11, F31.12, F31.13, F31.2, F31.31, F31.32, F31.4, F31.5, F31.73, F31.74, F31.75, F31.76, F31.9. Patients were selected in the non-bipolar cohort if they did not have any documented diagnosis for bipolar disorder: ICD-9/ICD-10 codes: 296.0x, 296.1x, 296.4x, 296.5x, 296.6x, 296.7x, 296.8x, 296.9x, 301.13/F30.xx, F31.xx, F34.xx, and F39.xx.

costs ranged from \$101.2 to \$124.3 billion.

4. Discussion

The results of this study showed that, in 2015, BDI was associated with a significant economic burden from a US societal perspective. More specifically, the total and excess costs associated with BDI were estimated at \$202.1 and \$119.8 billion, respectively. While the contribution of each cost component was different for total and excess costs, the largest contributors to both cost estimates were found to be caregiving costs, direct healthcare costs, and unemployment costs.

This study adds to the body of literature on the economic burden of BDI as the few existing studies assessing the costs associated with BD or BDI were based on data from over 20 years ago or focused on a limited number of cost components (Begley et al., 2001; Dilsaver, 2011; Wyatt and Henter, 1995). One of these previous studies (Wyatt and Henter, 1995) estimated the direct and indirect costs associated with “manic-depressive illness”, defined as BDI and BDII, in 1991, at \$45 billion using a prevalence of 1.3%. Although their estimate is lower than the one reported in the current study – even when accounting for

population growth and cost inflation – differences in studied populations, methodology, and years of data collection make direct comparisons particularly challenging. For example, the study by Wyatt and Henter (1995) relied on sources that did not distinguish between the costs associated with BD and those associated with other conditions such as affective disorders or schizophrenia. Furthermore, the definition of BD was based on the third version of the DSM (American Psychiatric Association, 1980), which included only two types of BD (American Psychiatric Association, 1980); conversely, the most recent, fifth version of the DSM, which was used for the present study, recognizes the existence of four subtypes of BD (American Psychiatric Association, 2013). In addition, contrary to the current study, healthcare costs were estimated based on aggregated estimates instead of patient-level data (e.g. pharmacy costs were only calculated for lithium prescriptions).

Another study (Begley et al., 2001) estimated direct and indirect costs associated with BD in 1998, assessing the lifetime costs of approximately 95,000 incident cases of BD (vs. 2,477,737 prevalent cases of BDI in the current study) based on the average age of disease onset and the probability of survival for each year of age. Although the

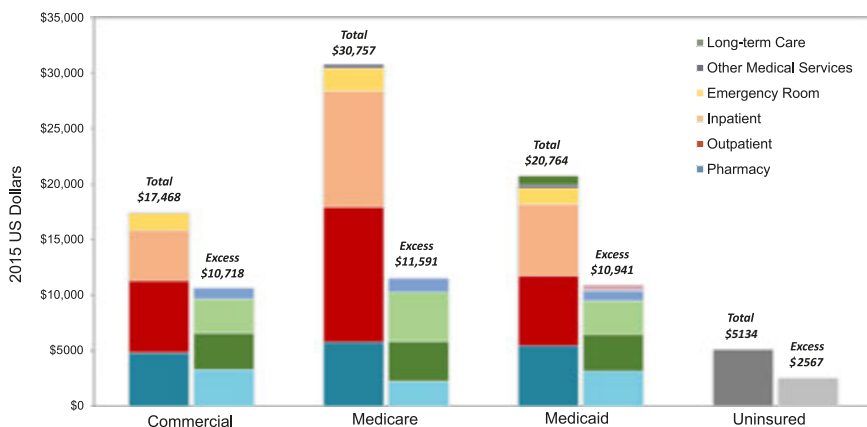


Fig. 2. Direct Total and Excess Healthcare Costs per Patient with Bipolar I Disorder in the United States in 2015. Excess costs were calculated as the difference between the direct healthcare costs incurred by the BDI cohort versus those of the non-BD cohort. Costs by component for uninsured individuals were not available in the literature. Long-term care costs were only available for Medicaid insured patients. Other medical services included services not included in other components such as durable medical equipment, skilled nursing services, home care services, and laboratory services. Costs were adjusted to 2015 US dollars using the Consumer Price Index.

authors also found a substantial economic burden of \$24 billion, our cost estimates cannot be compared with theirs due to major differences in the studied populations, cost components, and methods used. More recently, a study (Dilsaver, 2011) estimated the 2009 economic burden of BDI at \$71.9 billion adjusting the 1991 cost estimates from Wyatt and Henter (1995) for population growth, BDI prevalence, and CPI. However, by using the same data and assumptions as the Wyatt and Henter (1995) study, these estimates did not take into account any of the changes that have occurred in the clinical management and classification of BD over the past two decades.

Indeed, since the 1990s, the understanding of BD has improved and the treatment landscape evolved, particularly thanks to the addition of antipsychotics – mostly used in combination with lithium (Jann, 2014) – to the treatment armamentarium for BD (Gitlin and Frye, 2012; Harrison et al., 2016). In addition, legislation changes in the US have impacted both health plan coverage and quality of care for mental illness, likely affecting the costs associated with BDI. For instance, since 2006, the Medicare program includes prescription outpatient drug benefits (“Part D”), while the 2008 Mental Health Parity and Addiction Equity Act and the 2010 Patient Protection and Affordable Care Act have improved access to care for people with mental disorders (McGinty et al., 2015; Park et al., 2008; US Department of Labor, 2010). For instance, the overall uninsured rate in the US decreased by almost one half (from 16.0% in 2010 to 9.1%) in 2015, the most important reduction in the uninsured rate since the creation of Medicare and Medicaid more than five decades ago (Obama, 2016).

Because all these changes have likely impacted the medical and non-medical costs sustained by individuals with BDI over the course of the past 20 years, assessing the current total and excess costs of BDI is particularly important to better understand the magnitude of the resources that are being spent on BDI from a societal perspective. This is especially relevant as the excess economic burden of BDI is on par with that of a severe mental disease such as schizophrenia – estimated at \$155 billion in 2013 (Cloutier et al., 2016) – and only about two times lower than diabetes – estimated at \$245 billion in 2012 (American Diabetes Association, 2013) – a disease that is nearly ten times more prevalent than BDI (Menke et al., 2015). While BDI may not be as recognized as diabetes or considered as severe as schizophrenia, the results of this study indicate that it is nevertheless associated with considerable societal costs. In particular, the magnitude of indirect and direct non-healthcare costs, representing over three quarters of the estimated economic burden, call attention to the need for more effective treatment options for patients with BDI.

Several limitations should be taken into account when interpreting the result presented in this study. First, the BDI prevalence of 1.0% may be conservative as individuals with mental illnesses may be less likely to participate in studies and surveys or seek medical help (Kessler et al., 2005b). Second, direct healthcare costs were calculated based on patients with a recorded diagnosis of BDI. Therefore, patients with BDI, but not yet diagnosed, were not included in the study sample; these patients may have different characteristics from the diagnosed patients included in the analysis. Third, the requirement to have continuous insurance coverage for 12 months may have resulted in excluding patients with recurrent coverage gaps. Fourth, direct healthcare costs may not fully reflect the total societal costs as some of the costs may not be captured for administrative reasons. Fifth, because there is no single data source for BDI-related costs, several estimates from the literature and governmental publications were combined. While adjustments were conducted to account for inflation and potential characteristic differences between the US population and samples from data sources, adjustments were limited by the information available; thus, inconsistencies may remain across data sources. Sixth, this study was based on a US population; conclusions may not be generalizable to other countries. Lastly, when estimates for BDI were not available, estimates for BD were assumed to apply to BDI as well.

5. Conclusion

The current study provides a much needed update on the costs associated with BDI from a societal perspective. Importantly, the burden of BDI was found to go beyond direct healthcare costs as it was associated with substantial direct non-healthcare and indirect costs. This suggests that more effective treatments and practices are needed to reduce the economic and disease burdens of BDI on society.

Author statement

All authors, including those within the funding sources, collaborated on the interpretation of the data, writing of the manuscript, and decision to submit the paper for publication.

Acknowledgments and contributors

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Conflict of interest statement

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Conflicts of interest

Martin Cloutier, Annie Guerin, and Eric Wu are employees of Analysis Group, Inc., which has received consulting fees from Otsuka Pharmaceutical Development & Commercialization, Inc. and Lundbeck, for this study. Mallik Greene is an employee of Otsuka Pharmaceutical Development & Commercialization Pharmaceutical, Inc. Maelys Touya is an employee of Lundbeck.

Role of the funding sources

The funding sources contributed to and approved the study design and received regular updates on the progress of the study but were not involved in data collection or analysis.

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