

# It is illegal to post this copyrighted PDF on any website. The Economic Burden of Schizophrenia in the United States

Aditi Kadakia, MS<sup>a,\*</sup>; Maryaline Catillon, PhD<sup>b</sup>; Qi Fan, MS<sup>a</sup>; G. Rhys Williams, PhD<sup>a</sup>;  
Jessica R. Marden, ScD<sup>c</sup>; Annika Anderson, MPH<sup>b</sup>; Noam Kirson, PhD<sup>c</sup>; and Carole Dembek, MS<sup>a</sup>

## ABSTRACT

**Aim:** The economic burden of schizophrenia in the United States (US) was estimated at \$155.7 billion in 2013. Since 2013, the US experienced significant health care reforms and treatment advances. This study analyzed recent data and literature to update the US economic burden estimate for schizophrenia.

**Methods:** Direct and indirect costs associated with schizophrenia were estimated using a prevalence-based approach. Direct health care costs were assessed retrospectively using an exact matched cohort design in the IBM Watson Health MarketScan databases from October 1, 2015, through December 31, 2019. Patients with schizophrenia (identified using *ICD-10-CM* codes F20 and F25) were exactly matched to controls on demographics, insurance type, and index year. Direct non-health care costs were estimated using published literature and government data. Indirect costs were estimated using a human capital approach and the value of quality-adjusted life-years lost. Cost offsets were estimated to account for basic living costs avoided. Excess costs, comparing costs for individuals with and without schizophrenia, were reported in 2019 USD.

**Results:** The estimated excess economic burden of schizophrenia in the US in 2019 was \$343.2 billion, including \$251.9 billion in indirect costs (73.4%), \$62.3 billion in direct health care costs (18.2%), and \$35.0 billion in direct non-health care costs (10.2%). The largest drivers of indirect costs were caregiving (\$112.3 billion), premature mortality (\$77.9 billion), and unemployment (\$54.2 billion). Cost offsets, representing \$6.0 billion (1.7%), were subtracted from direct non-health care costs.

**Conclusions:** The estimated burden of schizophrenia in the US doubled between 2013 and 2019 and was \$343.2 billion in 2019, highlighting the importance of effective strategies and treatment options to improve the management of this difficult-to-treat patient population.

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<sup>a</sup>Sunovion Pharmaceuticals, Marlborough, Massachusetts

<sup>b</sup>Analysis Group, Inc., New York, New York

<sup>c</sup>Analysis Group, Inc., Boston, Massachusetts

\*Corresponding author: Carole Dembek, MS, Sunovion Pharmaceuticals, 84 Waterford Dr, Marlborough, MA 01752 (carole.dembek@sunovion.com).

Schizophrenia is a chronic, severe, and disabling mental health disorder affecting 1.19% of the US population and is characterized by deficits in thought processes, perceptions, and emotional responsiveness, leading to loss of function and autonomy.<sup>1–4</sup> Adults with schizophrenia in the US are more than 3.5 times as likely to die compared to adults in the general population, with cardiovascular risk factors, tobacco use, and substance abuse contributing to this excess mortality burden.<sup>5</sup>

Schizophrenia is associated with significant economic burden, not only for patients but also for families, other caregivers, and the wider society. In the US, the annual cost of schizophrenia was estimated to be greater than the annual costs of all cancers combined.<sup>6</sup> The costs of schizophrenia can be characterized as direct health care, direct non-health care, and indirect costs. Direct health care costs include inpatient, outpatient, emergency department, long-term care, pharmacy costs, and costs related to other medical care (eg, community-based, nursing-home, and rehabilitation).<sup>7</sup> Direct non-health care costs typically include costs associated with law enforcement, homeless shelters, other social services, and research and training costs.<sup>7,8</sup> The indirect costs of schizophrenia are frequently defined as costs related to unemployment, lost productivity, caregiving, and premature mortality.<sup>7</sup>

A recent estimate of the overall cost burden of schizophrenia was published in 2016.<sup>8</sup> Cloutier et al estimated the annual US societal cost of schizophrenia in 2013 at approximately \$155.7 billion (excess direct health care costs: \$37.7 billion; direct non-health care costs: \$9.3 billion; indirect costs: \$117.3 billion; cost offsets: \$8.6 billion). Using a prevalence-based approach, Cloutier et al estimated incremental health care costs by insurance type (ie, Medicare, Medicaid, commercially insured, and uninsured) compared to matched control patients without schizophrenia. In addition, direct non-health care costs of law enforcement, homeless shelters, and research and training as well as indirect costs of unemployment, reduced work productivity, premature mortality, and caregiving were estimated.

The 2013 estimate of the US cost burden of schizophrenia does not reflect recent health care system reforms and treatment advances in schizophrenia. The Patient Protection and Affordable Care Act, enacted in 2010, reduced the proportion of uninsured adults from 18% in 2013 to 8% in 2019<sup>9,10</sup> and an estimated 15 million US residents gained Medicaid coverage over the same period.<sup>11</sup> Furthermore, the transition to the *International Classification of Diseases, 10th Revision (ICD-10)*, on October 1, 2015, resulted in new billing codes that may affect the coding of diagnoses of schizophrenia. Antipsychotic treatment options for patients with schizophrenia also changed since 2013, with new antipsychotics approved (eg, brexpiprazole, cariprazine, lumateperone, and aripiprazole long-acting injectable) and others going off patent (eg,

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### Clinical Points

- Estimating the burden of schizophrenia is complex, and past assessments of the burden of schizophrenia have not been updated to account for recent health care system reforms and treatment advances in schizophrenia.
- There is a need for effective treatment options and strategies to improve the management of schizophrenia.

quetiapine, olanzapine, and oral aripiprazole), thus affecting direct pharmacy costs.

Updated estimates of the societal economic burden of schizophrenia may increase awareness of the current burden of schizophrenia and inform future health care spending decisions. This study updated the prior 2013 analysis to estimate the total societal economic burden of schizophrenia in the US in 2019.

### METHODS

This study updated and refined the methodology described by Cloutier et al<sup>8</sup> to estimate the economic burden of schizophrenia in the US using a prevalence-based approach. A lifetime prevalence of 1.19% was used as the base case.<sup>3</sup> Sensitivity analyses were conducted using a lifetime prevalence of 0.72%.<sup>3</sup>

Excess costs represent the difference in costs between the population with schizophrenia and a similar population without schizophrenia. The total economic burden was estimated as the sum of excess direct health care costs, excess direct non-health care costs, and excess indirect costs, after subtracting the direct cost offsets.

Direct health care costs (pharmacy, outpatient care, inpatient care, emergency department visits, long-term care, and other medical services), direct non-health care costs (law enforcement, research and training, homeless shelters, and Supplemental Security Income [SSI] and Social Security Disability Insurance [SSDI]), direct cost offsets (basic living costs avoided by institutionalized individuals who would otherwise resort to the social safety net), indirect costs (unemployment, productivity loss, premature mortality, and caregiving), and overall costs were estimated using the most recent data available prior to the COVID-19 pandemic (to reflect a typical year of care), with all costs expressed in 2019 US dollars (USD).

Specific methods for the calculation of direct health care costs, and each dimension of direct non-health care and indirect costs, are described in the following section and in Table 1.

### Direct Health Care Costs

Direct health care costs for insured patients were estimated retrospectively using an exact matched cohort design, comparing patients with (case cohort) and without schizophrenia (control cohort). Insurance claims data from the IBM Watson Health MarketScan databases (October 1, 2015, through December 31, 2019) were used to group

patients into 3 samples: Medicaid-insured patients from the Multi-State Medicaid Database, commercially insured patients from the Commercial Claims and Encounters Database, and Medicare-insured patients from the Medicare Supplemental Database. This study was exempt from review by an institutional review board because the data were deidentified and compliant with the patient confidentiality requirements of the Health Insurance Portability and Accountability Act.

Patients were required to have continuous health plan enrollment for  $\geq 12$  months. The study period was defined as the last 12-month period available in the data, while the index date was defined as the last calendar date followed by 12 months of continuous enrollment in a health plan (ie, the last calendar date before the study period). Medicaid-insured and commercially insured patients were required to be  $\geq 18$  years old and  $< 65$  years old at the index date, while Medicare patients were required to be  $\geq 65$  years at the index date. In addition, patients included in the schizophrenia cohorts were required to have  $\geq 2$  diagnoses of schizophrenia (*ICD-10-CM* code: F20) or a schizoaffective disorder (*ICD-10-CM* code: F25) and were exactly matched to patients without schizophrenia on a ratio of up to 1:3 on age, sex, region of residence (commercial and Medicare only), race (Medicaid only), health plan type, and year of index date.

Patient characteristics were summarized descriptively for each payer population and included age, race, sex, insurance type, region, and index year, when available. Total direct health care costs for insured patients were estimated over the study period. Excess direct health care costs were based on the costs incurred by schizophrenia patients compared to non-schizophrenia patients in each payer population. Total excess health care costs for uninsured patients were calculated assuming a mean annual cost of \$909 per uninsured patient (\$800 in 2011 USD inflated to 2019 dollars)<sup>47</sup> and a cost ratio between patients with and without schizophrenia similar to the cost ratio observed in the Medicaid-insured population. Frequencies and proportions were reported for categorical variables, while means, standard deviations (SDs), medians, and interquartile ranges (IQRs) were reported for continuous variables.

### RESULTS

#### Total Economic Burden

Given a prevalence estimate of 1.19%, the schizophrenia population in the US in 2019 was estimated to be 3,906,050, contributing to an excess economic burden of \$343.2 billion (Figure 1, Table 2), which corresponded to an annual excess cost per person with schizophrenia of \$87,856. The excess direct health care costs were \$62.3 billion (\$15,957 per person with schizophrenia), the excess direct non-health care costs were \$35.0 billion (\$8,956 per person with schizophrenia), and the excess indirect costs were \$251.9 billion (\$64,479 per person with schizophrenia) (Figure 1). Costs associated with caregiving were the greatest contributor to excess indirect costs at \$112.3 billion (\$28,761 per person with

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**Table 1. Summary of Methods to Estimate Excess Cost Components**

Item	Components	Calculations
<b>Excess Direct Non-Health Care Costs</b>		
<b>Law Enforcement</b>		
Incarceration	Excess number of inmates with schizophrenia: 186,873 (calculated) <sup>12-15</sup> Excess cost of housing/caring for schizophrenia inmates (in millions): \$12,192 (calculated) <sup>16</sup> Excess rate of solitary confinement in mentally ill inmates: 10.80% <sup>17</sup> Excess cost of solitary confinement in schizophrenia inmates (in millions): \$1,095 (calculated) <sup>18</sup>	Calculated by multiplying the schizophrenia population by the sum of (1) the excess rate of incarceration in schizophrenia patients multiplied by the total cost of incarceration in non-mentally ill inmates (excess cost from excess incarceration rate), (2) the rate of incarceration in the schizophrenia population multiplied by the excess cost of incarceration in the schizophrenia population (excess cost conditional on being in jail), and (3) the excess rate of solitary confinement in mentally ill inmates multiplied by the excess cost of solitary confinement (excess cost of solitary confinement)
Legal and judicial services	Judicial and legal expenditures, adjusted for inflation and population growth (in millions): \$70,001 (calculated) <sup>19,20</sup> Excess rate of arrests: 6.57% <sup>21,22</sup>	Calculated by multiplying the total annual judicial and legal costs by the excess rate of arrest in the schizophrenia population The estimated number of arrests in the schizophrenia population was calculated by multiplying the number of individuals with schizophrenia at risk of arrest by the rate of arrest in the schizophrenia population
Police protection	Average police costs per crime: \$8,275 (calculated) <sup>23,24</sup> Excess number of crimes against schizophrenia population: 989,215 (calculated) <sup>22</sup>	Calculated by multiplying the average police protection cost per crime by the estimated excess annual number of crimes against the schizophrenia population. Average police cost per crime was estimated as the total police costs, inflated to 2019 USD and adjusted for population growth, divided by the total number of crimes in the US in 2019. Excess number of crimes against the schizophrenia population was calculated by multiplying the excess rate of victimization in the schizophrenia population by the number of individuals with schizophrenia
Schizophrenia-related research and training	National Institutes of Health schizophrenia-related research and training costs in the US population, 2019 (in millions): \$263 <sup>25</sup>	Reported by the National Institutes of Mental Health
Homeless shelters	Excess number of schizophrenia patients in homeless shelters: 139,410 (calculated) <sup>26,27</sup> Daily cost of providing shelter to a homeless person: \$41.57 (calculated) <sup>27,28</sup>	Estimated by multiplying the excess number of schizophrenia patients in shelters by the annual cost of sheltering a homeless individual. Excess number of homeless individuals with schizophrenia was calculated by multiplying the schizophrenia population by the excess rate of homelessness in the schizophrenia population. Annual cost of sheltering a homeless individual was extracted from the literature and inflated to 2019 USD
SSI and SSDI	Excess number of schizophrenia patients receiving SSI: 353,580 (calculated) <sup>29</sup> Average annual SSI payment/schizophrenia patient: \$7,317 (calculated) <sup>29</sup> Excess number of schizophrenia patients receiving SSDI: 351,116 (calculated) <sup>30</sup> Average annual SSDI payment/schizophrenia patient: \$11,234 (calculated) <sup>30</sup>	Calculated by multiplying the excess number of schizophrenia patients receiving SSI by the annual SSI payment per schizophrenia patient, added to the excess number of schizophrenia patients receiving SSDI multiplied by the annual SSDI payment per schizophrenia patient
	Components	Methods
<b>Excess Indirect Costs</b>		
Unemployment	Schizophrenia employment rate: 30.10% <sup>31</sup> Rate of employment in the non-schizophrenia population: 72.40% (calculated) <sup>31-33</sup> Excess number of unemployed in the schizophrenia population: 1,012,508 (calculated) <sup>31-33</sup> Mean annual income in the US: \$53,490 <sup>31</sup>	Estimated by multiplying the excess number of unemployed individuals in the schizophrenia population, derived from the rates of employment in the schizophrenia and schizophrenia-free populations, by the mean annual income in the United States
Productivity loss	Predicted income if patients did not have schizophrenia (in millions) <sup>31,32,34-36</sup> : Male: \$16,892 (calculated) Female: \$12,083 (calculated) Estimated income in the schizophrenia population (in millions) <sup>35,36</sup> : Male: \$10,629 (calculated) Female: \$10,927 (calculated)	Calculated as the difference between the median annual income of employees with and without schizophrenia in 2019, using published estimates of schizophrenia-specific productivity weights across genders and age categories. The average loss in annual income was calculated by multiplying the productivity loss (for each gender and age category) by the estimated number of employees with schizophrenia
Premature mortality	Estimated excess number of premature deaths in the schizophrenia population: 21,878 (calculated) <sup>37</sup> Potential life lost per death: 28.5 years <sup>5</sup> ICER threshold: \$125,000 <sup>38</sup>	Estimated by multiplying the estimated excess number of premature deaths in the schizophrenia population in 2019, by the number of potential life years lost per death, and the value of 1 life year as determined by the ICER threshold
Caregiving	Average total annual hours lost through direct care: 2,393 (calculated) <sup>39,40</sup> US employment over population: 71.90% <sup>32,33</sup> Mean hourly income in US population: \$25.72 <sup>34</sup> Percentage of the schizophrenia population in regular contact with family caregivers: 65% <sup>41</sup>	Calculated by multiplying the population with schizophrenia in regular contact with family caregivers in 2019 by the prevalence of treatable and treatment resistant schizophrenia (respectively), the number of hours devoted to caregiving by family members for patients with treatment-resistant and treatable schizophrenia (respectively), the employment rate in the US population (to account for the fact that not all caregivers would be working otherwise), and the hourly income in the US population

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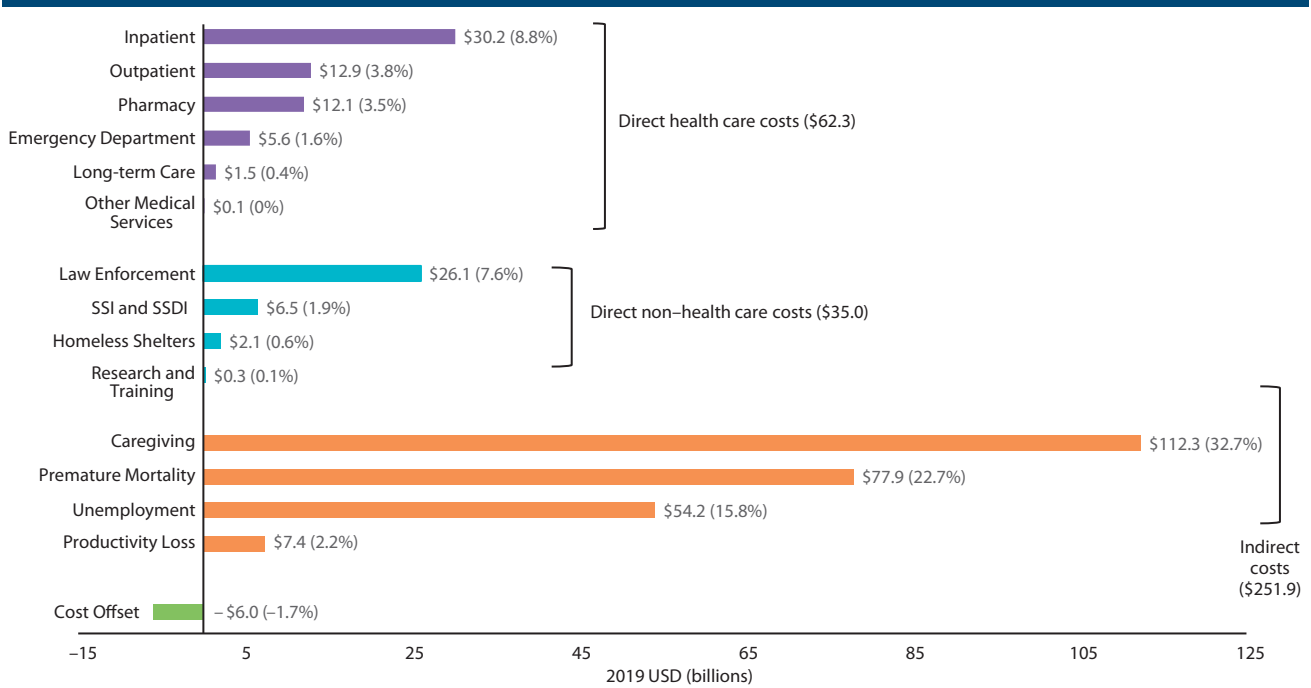
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Table 1 (continued).

Item	Components	Methods
<b>Direct Cost Offset</b>		
Cost offset	US poverty threshold for an individual in 2019: \$13,011 <sup>42</sup> Estimated excess number of individuals with schizophrenia not incurring basic living costs: 461,044 (calculated) <sup>12-15,26,27,43-46</sup> Psychiatric facilities: 26,018 (calculated) <sup>45,46</sup> Nursing homes: 98,743 (calculated) <sup>43,44</sup> Incarcerated: 186,873 (calculated) <sup>12-15</sup> Sheltered homeless: 139,410 (calculated) <sup>26,27</sup>	Calculated by multiplying the cost of living for a single person based on the US poverty threshold by the number of institutionalized individuals with schizophrenia who would otherwise resort to the social safety net (living in psychiatric facilities or nursing homes or are incarcerated or homeless)

Abbreviations: ICER=Institute for Clinical and Economic Review, PTSD= posttraumatic stress disorder, QALY= quality-adjusted life-year, SSDI= Social Security Disability Income, SSI= Supplemental Security Income.

Figure 1. Distribution of Excess Total Costs of Schizophrenia in the United States in 2019<sup>a</sup>



<sup>a</sup>Schizophrenia totaled an excess economic burden of \$343.2 billion in 2019. Of the total excess burden, excess direct health care costs, which accounted for pharmacy, outpatient, inpatient, emergency department, long-term care, and other medical services, totaled \$62.3 billion USD (18.2%). Excess direct non-health care costs consisted of law enforcement (incarceration, legal and judicial services, and police protection), schizophrenia-related research and training, homeless shelter costs, and SSI and SSDI and totaled \$35.0 billion USD (10.2%). Excess indirect costs included costs related to unemployment, productivity loss, premature mortality, and caregiving, totaling \$251.9 billion USD (73.4%). Cost offsets were included to exclude 461,044 institutionalized or homeless individuals not incurring basic living costs. All values were inflated to 2019 USD and were calculated assuming a disease prevalence of 1.19%. Abbreviations: SSDI= Social Security Disability Income, SSI= Supplemental Security Income.

schizophrenia), accounting for about a third of the total excess costs (Figure 1). Cost offsets, representing \$6.0 billion (\$1,536 per person with schizophrenia), were subtracted from direct non-health care costs.

**Excess Direct Health Care Costs**

Direct health care costs were estimated based on a sample of 131,125 patients with schizophrenia. Among these patients, 24,881 (19.0%) were commercially insured, 2,779 (2.1%) were Medicare-insured, and 103,465 (78.9%) were Medicaid-insured (Table 3). On average (mean values), patients were 37.3, 76.2, and 41.7 years old at index across the commercially insured, Medicare-insured, and

Medicaid-insured populations, respectively; most of the commercial and Medicaid population were male (56.0% and 53.3%, respectively) while most of the Medicare population (64.9%) were female (Table 3).

Excess direct health care costs were estimated to be \$62.3 billion and included costs associated with pharmacy (\$12.1 billion), outpatient care (\$12.9 billion), inpatient care (\$30.2 billion), emergency department visits (\$5.6 billion), long-term care (\$1.5 billion), and other medical services (\$120.6 million) (Table 2). Mean total health care costs were similar across the commercially insured and Medicaid-insured cohorts but were higher for Medicare-insured patients (\$26,904, \$26,095, and \$34,391, respectively) (Table 4).

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**Table 2. Total Excess Costs for Patients With Schizophrenia in the United States in 2019**

Component	Primary Analysis (1.19% Prevalence)		Sensitivity Analysis (0.72% Prevalence)	
	Costs, Millions	Proportion of Total Cost, %	Costs, Millions	Proportion of Total Cost, %
<b>Excess direct health care costs</b>				
Pharmacy	\$12,061	3.5	\$7,298	3.4
Outpatient	\$12,887	3.8	\$7,797	3.6
Inpatient	\$30,185	8.8	\$18,263	8.5
Emergency department	\$5,578	1.6	\$3,375	1.6
Long-term care	\$1,496	0.4	\$905	0.4
Other medical services	\$121	<0.1	\$73	<0.1
<b>Total excess direct health care costs</b>	<b>\$62,329</b>	<b>18.2</b>	<b>\$37,712</b>	<b>17.5</b>
<b>Excess direct non-health care costs</b>				
Law enforcement	\$26,072	7.6	\$21,173	9.8
Incarceration	\$13,286	3.9	\$13,492	6.3
Legal and judicial services	\$4,601	1.3	\$2,753	1.3
Police protection	\$8,185	2.4	\$4,929	2.3
Homeless shelters	\$2,116	0.6	\$2,172	1.0
Schizophrenia-related research and training	\$263	0.1	\$263	0.1
SSI and SSDI	\$6,532	1.9	\$7,181	3.3
<b>Total excess direct non-health care costs</b>	<b>\$34,983</b>	<b>10.2</b>	<b>\$30,790</b>	<b>14.3</b>
Cost offset	-\$5,999	-1.7	-\$6,242	-2.9
<b>Excess indirect costs</b>				
Unemployment	\$54,159	15.8	\$32,613	15.2
Productivity loss	\$7,418	2.2	\$4,488	2.1
Premature mortality	\$77,939	22.7	\$47,744	22.2
Caregiving	\$112,340	32.7	\$67,971	31.6
<b>Total excess indirect costs</b>	<b>\$251,857</b>	<b>73.4</b>	<b>\$152,816</b>	<b>71.1</b>
<b>Total Excess Costs</b>	<b>\$343,171</b>		<b>\$215,076</b>	

Abbreviations: SSDI=Social Security Disability Income, SSI=Supplemental Security Income.

Mean excess health care costs varied across cohorts, with the greatest excess among commercially insured patients (\$19,293), followed by Medicaid- and Medicare-insured patients at \$15,347 and \$11,963, respectively. The estimated excess cost per uninsured patient with schizophrenia was \$1,289, representing a total excess cost of \$411.9 million.

### Excess Direct Non-Health Care Costs

Excess direct non-health care costs were estimated to be \$35.0 billion, accounting for approximately 10.2% of the total economic burden of schizophrenia in 2019 (Figure 1, Table 2). Excess law enforcement costs were estimated to be \$26.1 billion, including \$8.2 billion in police protection, \$4.6 billion in judicial and legal services, and \$13.3 billion in incarceration costs. Excess homeless shelter costs were estimated to be \$2.1 billion, corresponding to homeless shelter costs for 139,410 excess sheltered homeless individuals with schizophrenia. Annual schizophrenia-related research and training costs were \$263.0 million, as reported by the National Institutes of Health.<sup>25</sup> Excess costs related to SSI and SSDI were estimated to be \$6.5 billion, accounting for mean annual SSI and SSDI payments of, respectively, \$7,317 and \$11,234 per schizophrenia patient.

### Excess Direct Cost Offsets

Based on an estimated 461,044 excess individuals with schizophrenia not incurring basic living costs in 2019, direct cost offsets of \$6.0 billion were deducted from the excess direct non-health care costs based on the US Census Bureau Poverty Threshold for an individual in 2019,<sup>42</sup> which was \$13,011 (Figure 1, Table 2).

### Excess Indirect Costs

Excess indirect costs accounted for 73.4% (\$251.9 billion) of the total economic burden of schizophrenia (Figure 1, Table 2). Costs associated with caregiving were the greatest contributor to excess indirect costs at an estimated \$112.3 billion, accounting for 32.7% of the total economic burden. Costs due to premature mortality, unemployment, and productivity loss totaled \$77.9 billion, \$54.2 billion, and \$7.4 billion, respectively.

### Sensitivity Analysis

Using a lifetime prevalence rate of 0.72%,<sup>3</sup> the schizophrenia population in the US in 2019 was estimated to be 2,363,325, contributing to an excess economic burden of \$215.1 billion (Table 2). Using this prevalence estimate, excess direct health care, direct non-health care, and indirect costs represented \$37.7 billion (17.5%), \$30.8 billion (14.3%), and \$152.8 billion (71.1%), respectively.

## DISCUSSION

The economic burden of schizophrenia in the US in 2019 was estimated at \$343.2 billion. Indirect costs accounted for over 73% of total costs and were largely driven by caregiving costs (\$112.3 billion), which accounted for about one-third (32.7%) of the total excess economic burden. These findings suggest that the total estimated burden of schizophrenia doubled (+100.9%) between 2013 and 2019 (after adjusting for inflation). On a per-patient basis, the burden increased by 78.8% (after adjusting for inflation), consistent with an overall increase in schizophrenia burden.

**Table 3. Patient Characteristics for Direct Health Care Costs in the United States**

Patient Characteristics <sup>a</sup>	Commercially Insured (n = 24,881)	Medicare-Insured (n = 2,779)	Medicaid-Insured (n = 103,465)
Age, y			
Mean ± SD	37.3 ± 14.6	76.2 ± 6.9	41.7 ± 13.0
Median (IQR)	33.9 (24.2–50.5)	74.5 (70.5–81.5)	41.5 (30.5–53.5)
Age groups			
≥ 18 to < 25	8,105 (32.6)	0 (0.0)	12,065 (11.7)
≥ 25 to < 35	4,684 (18.8)	0 (0.0)	24,797 (24.0)
≥ 35 to < 45	3,524 (14.2)	0 (0.0)	22,622 (21.9)
≥ 45 to < 55	4,100 (16.5)	0 (0.0)	22,240 (21.5)
≥ 55 to < 65	4,468 (18.0)	0 (0.0)	21,741 (21.0)
≥ 65 years	0 (0.0)	2,779 (100.0)	0 (0.0)
≥ 65 to < 75	0 (0.0)	1,422 (51.2)	0 (0.0)
≥ 75 to < 85	0 (0.0)	1,005 (36.2)	0 (0.0)
≥ 85 to < 95	0 (0.0)	339 (12.2)	0 (0.0)
≥ 95	0 (0.0)	13 (0.5)	0 (0.0)
Male	13,922 (56.0)	976 (35.1)	55,129 (53.3)
Race <sup>b</sup>			
Black	...	...	50,752 (49.1)
White	...	...	49,095 (47.5)
Hispanic	...	...	1,932 (1.9)
Other	...	...	1,686 (1.6)
Insurance type			
HMO	3,163 (12.7)	160 (5.8)	47,077 (45.5)
POS	2,776 (11.2)	129 (4.6)	0 (0.0)
POS	2,480 (10.0)	79 (2.8)	0 (0.0)
POS with capitation	296 (1.2)	50 (1.8)	0 (0.0)
Non-HMO/POS	18,942 (76.1)	2,490 (89.6)	56,388 (54.5)
CDHP	2,556 (10.3)	9 (0.3)	0 (0.0)
Comprehensive	1,369 (5.5)	1,505 (54.2)	56,388 (54.5)
EPO	183 (0.7)	0 (0.0)	0 (0.0)
HDHP	1,813 (7.3)	5 (0.2)	0 (0.0)
PPO	13,018 (52.3)	971 (34.9)	0 (0.0)
US Census region <sup>c</sup>			
South	10,622 (42.7)	724 (26.1)	...
Midwest	5,442 (21.9)	1,256 (45.2)	...
Northeast	4,913 (19.7)	613 (22.1)	...
West	3,864 (15.5)	186 (6.7)	...
Index year			
2015	425 (1.7)	47 (1.7)	1,265 (1.2)
2016	6,418 (25.8)	1,630 (58.7)	14,871 (14.4)
2017	5,612 (22.6)	587 (21.1)	9,493 (9.2)
2018	12,426 (49.9)	515 (18.5)	77,836 (75.2)

<sup>a</sup>Patient characteristics were reported as of the index date. The index date was defined as the last calendar date that was followed by 12 months of continuous health plan coverage. Continuous eligibility was defined as continuous enrollment in an insurance plan (commercial, Medicaid, or Medicare) and continuous prescription drug coverage. Values are shown as n (%) unless otherwise noted.

<sup>b</sup>Race was not available for commercially insured and Medicare-insured patients.

<sup>c</sup>US Census region was not available for Medicaid-insured patients.

Abbreviations: CDHP = consumer-driven health plan, EPO = exclusive provider organization, HDHP = high deductible health plan, HMO = health maintenance organization, IQR = interquartile range, POS = point-of-service, PPO = preferred provider organization.

A sensitivity analysis using a lower prevalence estimate of 0.72% estimated that the total burden increased by 25.9% between 2013 and 2019.

Compared to Cloutier et al<sup>8</sup> and after adjusting for inflation, direct health care costs were 50.7% higher (\$62.3 billion in 2019 vs \$41.4 billion in 2013). The increase in direct health care costs (+50.7%) was primarily driven by a \$13.5 billion increase in inpatient costs (+80.9%) and a \$4.8 billion increase in outpatient costs (+58.8%). Although other direct health care costs represented a smaller proportion of the overall increase, long-term care costs (+\$0.8 billion) and emergency department costs (+\$2.8 billion) doubled in 6 years (respectively, +124.5% and +97.8%), suggesting a potentially concerning trend.

Over the same period, pharmacy (drug) costs increased by 19.2% (+\$1.9 billion).

The difference in direct health care costs between Cloutier et al<sup>8</sup> and the current study can be attributed to several factors: the increase in the schizophrenia population (+12%), influenced by the increase in the US population and the difference in prevalence between the two studies (1.19% vs 1.10%); the change in per-patient excess costs among commercially insured patients (+41.1%), Medicaid patients (+12.4%), and Medicare patients (−12.1%); a decrease in the size of the uninsured US population between 2013 and 2019 and the assumed health care costs among uninsured patients (annual excess costs related to uncompensated care estimated at \$1,289 per patient versus assumed to be \$0).

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**Table 4. Annual 2019 Total Direct Health Care Costs per Schizophrenia Patient**

Direct Health Care Cost Component (2019 USD) <sup>a</sup>	Commercially Insured (n=24,881)	Medicare-Insured (n=2,779)	Medicaid-Insured (n=103,465)
<b>Total Costs</b>			
Mean ± SD	\$26,904 ± \$57,242	\$34,391 ± \$58,104	\$26,095 ± \$78,415
Median (IQR)	\$10,634 (\$3,060–\$28,868)	\$17,290 (\$6,236–\$40,982)	\$4,894 (\$175–\$28,552)
<b>Pharmacy Costs</b>			
Mean ± SD	\$5,579 ± \$14,103	\$5,614 ± \$9,826	\$5,557 ± \$14,312
Median (IQR)	\$1,294 (\$222–\$5,708)	\$2,462 (\$682–\$7,107)	\$240 (\$0–\$4,583)
<b>Medical Costs</b>			
Mean ± SD	\$21,325 ± \$54,516	\$28,777 ± \$56,716	\$20,539 ± \$75,385
Median (IQR)	\$5,145 (\$1,387–\$20,269)	\$10,226 (\$2,758–\$34,160)	\$2,496 (\$142–\$17,426)
<b>Outpatient Costs</b>			
Mean ± SD	\$7,320 ± \$23,921	\$11,889 ± \$26,015	\$8,867 ± \$28,028
Median (IQR)	\$2,238 (\$813–\$6,296)	\$4,419 (\$1,692–\$12,241)	\$1,104 (\$0–\$6,000)
<b>Inpatient Costs</b>			
Mean ± SD	\$11,488 ± \$41,165	\$13,964 ± \$41,335	\$6,814 ± \$64,795
Median (IQR)	\$0 (\$0–\$7,480)	\$0 (\$0–\$13,679)	\$0 (\$0–\$0)
<b>ED Costs</b>			
Mean ± SD	\$2,431 ± \$8,861	\$2,717–\$8,842	\$1,231 ± \$4,054
Median (IQR)	\$0 (\$0–\$1,782)	\$0 (\$0–\$2,146)	\$0 (\$0–\$882)
<b>Long-Term Care Costs<sup>b</sup></b>			
Mean ± SD	...	...	\$3,420 ± \$18,562
Median (IQR)	...	...	\$0 (\$0–\$0)
<b>Other Medical Service Costs<sup>c</sup></b>			
Mean ± SD	\$88 ± \$1,231	\$206 ± \$976	\$207 ± \$933
Median (IQR)	\$0 (\$0–\$0)	\$0 (\$0–\$84)	\$0 (\$0–\$71)

<sup>a</sup>Costs were measured from a societal perspective (ie, amounts reimbursed by payers and patients' out-of-pocket costs) during the study period and adjusted for inflation using the US Medical Care component of the Consumer Price Index inflation factor for medical care and were reported in 2019 USD. The study period was defined as the 12-month period following the index date. The index date was defined as the last calendar date that was followed by 12 months of continuous health plan coverage.

<sup>b</sup>Long-term care costs were not available in commercial and Medicare claims.

<sup>c</sup>Other medical service costs were defined as costs associated with durable medical equipment, dental care, and vision care. Abbreviations: ED = emergency department, IQR = interquartile range.

Direct non-health care costs and indirect costs were, respectively, 290.4% higher (\$39.8 billion in 2019 vs \$10.2 billion in 2013), and 95.7% higher (\$251.9 billion vs \$128.7 billion in 2013) than in Cloutier et al,<sup>8</sup> partially due to a change in methodology to estimate these excess costs more comprehensively. The increase in law enforcement costs (+293.1%) was driven by a higher victimization rate in the schizophrenia population from the literature (25.33% in current study vs 5.25% in Cloutier et al<sup>8</sup>), leading to a 6-fold increase in police protection costs. The calculation of incarceration costs in this study considered the excess rate of incarceration in the schizophrenia population as in Cloutier et al,<sup>8</sup> but also the excess cost of incarceration conditional on being in jail and the excess cost of solitary confinement. Direct non-health care costs also included SSI and SSDI, which constitute important sources of income for people living with schizophrenia but were not included in the 2013 estimate.<sup>48</sup>

The increase in indirect costs was driven by a 20-fold increase in the estimate of premature mortality costs (+\$74.3 billion) and by the doubling of caregiving costs (+\$54.7 billion). Cloutier et al<sup>8</sup> included only suicide-related premature mortality costs using a human capital approach. In contrast, the current study considered all premature mortality costs and valued life years lost at \$125,000 per life-year, the midpoint between \$100,000 and \$150,000 per quality-adjusted life-year gained, which is used by several value assessment organizations in the US.<sup>16</sup> As suicide-related costs constitute only a small proportion of the premature

mortality costs of schizophrenia, the current methods accounted for the burden of schizophrenia on premature mortality more comprehensively regardless of the direct cause of death. Concerning caregiving costs, the current study used a direct valuation approach (as in Cloutier et al<sup>8</sup>) along with updated estimates accounting for heterogeneity in caregiving time between patients with treatable and treatment-resistant schizophrenia. This is an important distinction, as these two subgroups of patients require very different caregiver involvement.<sup>17</sup> The updated estimate of caregiving time was based on peer-reviewed publications<sup>39,40</sup> (versus a news survey in Cloutier et al<sup>8</sup>).

In 2021, The Schizophrenia & Psychosis Action Alliance (SPAA) published a report<sup>48</sup> estimating the cost of schizophrenia in the US at \$281.6 billion in 2020 (versus \$343.2 billion in 2019 in this study), including \$27.2 billion in direct health care costs (versus \$62.3 billion), \$46.6 billion in direct non-health care costs (versus \$35.0 billion), and \$219.6 billion in indirect costs (versus \$251.9 billion; including caregiving [\$104.5 billion vs \$112.3 billion]).

The difference in costs between this study and the SPAA report is due to the use of a different prevalence estimate (0.8% versus 1.19% in this study) as well as different data sources and methodologies to estimate direct and indirect cost components. Much lower direct health care costs in the SPAA report (\$27.2 billion vs \$62.3 billion in this study) are due to the use of Medical Expenditure Panel Survey data (versus claims data), which rely on patient self-report and may underreport health care use as well as underrepresent

patients with high expenditures.<sup>18</sup> The large difference in costs for supportive housing and homelessness (\$24.7 billion vs \$2.1 billion in this study) is due to the incorporation of total costs for supportive housing in the SPAA report because excess costs could not be calculated. In the absence of the data necessary to calculate excess costs, this study did not include supportive housing costs (thus providing a conservative estimate). Indirect cost estimates, which included some of the largest contributors to the overall burden, including caregiving, premature mortality, and productivity loss, were generally consistent between the two studies despite the use of different data sources and methodologies.

### Limitations

This study utilized a prevalence-based approach. According to the National Institute of Mental Health (NIMH), precise estimates of schizophrenia prevalence are difficult to achieve due to its overlap with other disorders in presentation, clinical complexity, and inconsistent diagnostic methods.<sup>2</sup> The estimation of direct health care costs included both schizophrenia (*ICD-10-CM* code F20) and schizoaffective disorders (*ICD-10-CM* code F25). However, the estimation of direct non-health care costs and indirect costs is based on the literature, where the definition used for schizophrenia (including or excluding schizoaffective disorders) was not consistently available. Therefore, this estimate of the total excess burden of schizophrenia may under or overestimate the true burden of disease. To mitigate this concern, this study includes a sensitivity analysis using a 0.72% prevalence estimate in addition to the base case of 1.19%.

There may be wide variation in costs across patients with schizophrenia depending on severity of schizophrenia and the presence and severity of comorbidities. This study uses average costs as inputs to calculate excess costs, which accounts for the distribution of severity in the

population in the calculation of total costs. In addition, the study accounts for heterogeneity in costs within the schizophrenia population whenever possible; for example, caregiving costs consider the heterogeneity in caregiving time between patients with treatable and treatment-resistant schizophrenia.

This study estimates excess costs among individuals diagnosed with schizophrenia. Consequently, the direct health care costs among people with undiagnosed schizophrenia were not captured, thereby likely underestimating the excess burden of schizophrenia. Similarly, patients eligible for multiple insurance types (eg, Medicare and Medicaid) and those covered by military health insurance were not represented in this sample. Our analysis assumed that these individuals were similar to individuals included in our sample, which may limit the generalizability of the findings to these populations. Further, to estimate the direct health care costs in the uninsured population, it was assumed that the cost ratio observed in the Medicaid population between the schizophrenia and schizophrenia-free populations also applied to the uninsured population, which may not be the case. Finally, premature mortality was estimated using a life-year valuation approach and would change if different life-year valuations were used.

### CONCLUSION

The estimated societal burden of schizophrenia in the US in 2019 was \$343.2 billion, representing a 100.9% increase in the estimated burden from 2013 to 2019 (inflation adjusted). Indirect costs contributed the most to the overall economic burden of disease, driven largely by costs associated with caregiving (\$112.3 billion), which accounted for about a third of the total economic burden. The large societal burden of schizophrenia in the US highlights the importance of effective strategies and treatment options to improve the management of this difficult-to-treat patient population.

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**IRB:** This study was exempt from review by an institutional review board because the data were de-identified and compliant with the patient confidentiality requirements of the Health Insurance Portability and Accountability Act.

**Additional information:** The data used for the present study were licensed by Analysis Group, Inc., from IBM Watson and are not publicly available. Further information on the IBM MarketScan

databases can be found at <https://www.ibm.com/products/marketscan-research-databases>.

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