

The Financial Impact of Ehlers-Danlos Syndromes on Patients in the United States in 2022

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Abstract

Objective: To determine the financial impact of Ehlers-Danlos syndromes (EDS) on patients in the United States by examining the medical expenses incurred by patients.

Patients and Methods: We used a convenience sample approach and disseminated a self-reported survey questionnaire to individuals with EDS via patient advocacy organizations and support groups across the country, social media, and health professionals from April 1, 2023, to December 31, 2023. The survey focused on the out-of-pocket medical expenses incurred by patients.

Results: The final analytic data set included 884 responses. Responses were received from individuals in all 50 states and the District of Columbia. More than 50% reported individual income less than \$25,000, and more than 30% reported household income less than \$50,000. More than 80% of respondents had some type of commercial insurance and 29% reported receiving Medicaid. Respondents received more financial assistance from their family and friends than from government sources. The total median out-of-pocket financial cost by our analysis was \$13,450 (IQR: \$6500-\$25,800). Of the 838 who responded to the question, "Did the affected person receive the health care they needed?", 19% answered "no", 51% answered "yes, sometimes", and 30% answered "yes, most of the time".

Conclusion: The factors contributing to financial impact include both direct and indirect costs of accessing and receiving medical care. Our study findings highlight the magnitude of the burden of health care spending on patients with EDS.

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Ehlers-Danlos syndromes (EDS) are a group of heritable disorders of connective tissue characterized by varying degrees of joint hypermobility and instability, skin hyperextensibility and scarring, and other tissue fragilities that may lead to vascular and visceral rupture.¹ Other systemic manifestations include sleep disturbance, fatigue, postural orthostatic tachycardia, functional gastrointestinal disorders, dysautonomia, anxiety, and depression. These other symptoms may be even more debilitating than the joint symptoms, often impair functionality and quality of life¹ and, if not treated, can lead to chronic complex multisystem concerns, requiring multidisciplinary care by medical, surgical, and therapy specialties.²

People with EDS have significant health challenges; however, their impact in terms of

utilization and cost is not well known. Factors that have economic impact include highly variable symptoms and treatment needs, treatment is typically managed by multiple providers, and it often takes a long time to get diagnosed.

Research goals

The primary objective of this study was to determine the financial impact of EDS to patients in the United States. This study reports the direct out-of-pocket (OOP) medical costs incurred by patients, as well as indirect costs.

PATIENTS AND METHODS

Survey Questionnaire Design and Dissemination

The study design was a patient self-reported online survey questionnaire. We constructed

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a survey questionnaire using a previous questionnaire as a model. This questionnaire was prepared for the EveryLife Foundation by the Lewin Group, published in the *National Economic Burden of Rare Diseases Study*, February 2021.³ We modified the survey questionnaire to make it applicable to the EDS patient population. The purpose of the questionnaire was to gather the estimated financial costs related to EDS medical care incurred by patients for the year 2022. The questionnaire included demographic characteristics, diagnosis, functional status, financial resources, and health care spending.

We used a convenience sample approach and disseminated our survey to individuals with EDS via patient advocacy organizations and support groups across the country, social media, and health professionals. The patient advocacy organizations included more than 20 support groups in the United States that were listed on the Ehlers-Danlos Society website. The representatives of these groups were asked to distribute an online link to our study's questionnaire through their social media groups and newsletters. A brochure describing the study was made available in the waiting room of 1 outpatient rehabilitation center at our institution. We did not send individual surveys to patients or health care professionals. Health care professionals were not part of the study and, therefore, did not complete questionnaires. We included hypermobility spectrum disorder as a diagnosis choice in the survey because patients with hypermobility spectrum disorder have joint hypermobility and are known to experience many of the same comorbid medical conditions as persons with the hypermobile type of EDS.⁴⁻⁶ We did not assess other diagnoses. The diagnoses were self-reported. Diagnosis verification was not part of the study design because the survey questionnaires were anonymous. The survey was active from April 1, 2023, to December 31, 2023.

This research study was approved by the Pennsylvania State University Institutional Review Board, Human Research Protection Program (STUDY# 00022037, February 6, 2023). The research met the criteria for exempt research according to the policies of this institution and the provisions of applicable federal regulations.

Data Analysis

Preparing the Study Data Set. Data set preparation and cleaning included establishing methods to handle missing data and errors. Some of the survey response entries were obvious errors (eg, 50,000 primary care visits). We used a previous data set, a MarketScan sample for the calendar year 2021,⁷ to establish reasonable criteria to set responses to missing. This resulted in the following ranges used for utilization variables:

- Number of primary care visits (0-150)
- Number of specialty care visits (0-150)
- Number of physical/occupational therapy visits (0-200)
- Number of other therapy visits (0-200)
- Number of emergency department visits (0-50)
- Number of hospital admissions (0-50)
- Number of operations (0-35)

Responses greater than the upper range were set to be missing for the analysis.

OOP direct expenses were the sum of the following 17 items survey items:

- Health insurance premiums
- Health insurance deductibles
- Copayments or coinsurance for physician office visits, emergency department visits, or hospital admissions
- Prescription medications
- Diagnostic tests
- Genetic counseling or genetic tests
- Alternative or nontraditional treatments
- Mental health treatments, including counseling
- Physical/occupational/speech therapy
- Routine dental care
- Routine eye care
- Oral operation, care, and services
- Over-the-counter drugs
- Medical foods
- Vitamins, calorie concentrates, and other supplements
- Specialty clothing, such as compression stockings or garments
- Equipment such as braces, collars, splints, night guards

If ≥ 3 items were missing from the above-mentioned list, then OOP direct expenses

TABLE 1. Demographic characteristics, EDS Diagnosis Type, Year Diagnosed

	<i>n</i>	%
Sex at birth		
Male	33	3.7
Female	842	95.2
Prefer not to answer	9	1.0
Race		
American Indian or Alaska Native	11	1.2
Asian	6	0.7
Black or African American	4	0.5
Multiracial	30	3.4
White or Caucasian	796	90.4
Prefer not to answer	34	3.8
Missing	3	
Ethnicity		
Hispanic	45	5.3
Non-Hispanic	786	91.9
Prefer not to answer	24	2.8
Missing	29	
Highest level of education		
Less than a high school diploma	10	1.1
High school diploma	49	5.6
Some college (1-4 years, no degree)	164	18.7
Associate's or Bachelor's degree	343	39.0
Master's degree	219	24.9
PhD or professional school degree	73	8.3
Prefer not to answer	21	2.4
Missing	5	
Marital status		
Married	432	49.3
Unmarried but living with partner	92	10.5
Widowed	10	1.1
Divorced/separated	103	11.7
Single, never married	212	24.2
Prefer not to answer	28	3.2
Missing	7	
Type of EDS		
Hypermobility EDS	736	84.0
Vascular EDS	14	1.6
Classical EDS	27	3.1
Classical-like EDS	11	1.3
Arthrochalasia EDS	2	0.2
Dermatosparaxis EDS	1	0.1
Kyphoscoliotic EDS	6	0.7
Spondylodysplastic EDS	1	0.1
Musculoskeletal EDS	1	0.1
Myopathic EDS	3	0.3
Periodontal EDS	4	0.5
Combination, mixed types EDS	16	1.8
Hypermobility spectrum disorder	28	3.2
Unknown or not sure	26	3.0
Missing	8	

Continued on next column

TABLE 1. Continued

	<i>n</i>	%
Year EDS diagnosed (N=810 with known year)		
2013 and earlier	146	18.0
2014-2018	221	27.3
2019-2023	443	54.7

EDS, Ehlers-Danlos syndrome.

were considered missing. Otherwise, if 1 or 2 were missing (<15%), then missing items were assumed to have \$0 in costs.

OOP other expenses were the sum of the following 8 survey items:

- Expenses related to purchasing equipment (such as pulse oximeter)
- Purchasing/installing/modifying special equipment at home
- Home modifications
- Purchasing/installing/modifying a personal family vehicle
- Hiring someone for providing EDS-related daily care
- Hiring someone to provide daily care to other household members owing to reduced functional ability
- Transportation costs related to medical care for EDS
- Travel-related expenses incurred because of EDS

If ≥2 items were missing from the above-mentioned list, then OOP other expenses were considered missing. Otherwise, if only 1 item was missing (12.5%), then the missing item was assumed to have \$0 in costs.

We categorized type of insurance as private, public, and none. If individual coverage or family coverage was selected for commercial insurance through own or spouse's employer or individual commercial insurance (private), then the insurance was classified as private. Otherwise, if any of the other insurance were selected (individual health insurance purchased through a state or federal exchange through Military/CHAMPUS/TRICARE/VA health care program), then the insurance was classified as public.

Functional status was on the basis of a list of 27 items. Participants were asked whether EDS currently limits the ability to do any of the activities using the following scale: 4,

TABLE 2. Individual and Household Income in the Year 2022

N=884	Total earnings, affected person, n (%)	Household income, n (%)
None or insignificant	226 (25.9)	52 (6.2)
\$1000 to <\$25,000	239 (27.3)	92 (10.9)
\$25,000 to <\$50,000	140 (16.0)	122 (14.5)
\$50,000 to <\$75,000	109 (12.5)	122 (14.5)
\$75,000 to <\$100,000	64 (7.3)	122 (14.5)
\$100,000 to <\$150,000	43 (4.9)	145 (17.2)
More than \$150,000	27 (3.1)	156 (18.5)
Prefer not to answer, do not know, not applicable	24 (2.8)	31 (3.7)
Missing	10	42

able to do; 3, some limitations; 2, significant limitations; 1, completely unable; and 0, not applicable. We defined functional status as the number of items answered as completely unable or significant limitations. Thus, the score for functional status can range from 0 (no limitations) to 27 (limitations for all items). If ≥ 3 items were missing ($>11\%$), then functional status was considered

TABLE 3. Insurance Coverage, 2022 (Individual and/or Family)

	No. of missing	No. (%) of nonmissing
Commercial insurance through own or spouse's employer	141	530 (71.3)
Individual commercial insurance (private)	333	56 (10.1)
Individual health insurance purchased through a state or federal exchange	322	78 (13.8)
Medicaid/SCHIP	296	171 (29.1)
Medicaid Waiver program (eligibility through the Tax Equity and Fiscal Responsibility Act (TEFRA)/Katie Beckett Waivers)	356	15 (2.8)
Medicare Part A (Hospital Insurance)	300	129 (22.1)
Medicare Part B (Medical Insurance)	300	125 (21.4)
Medicare Part C (Medicare Supplemental Insurance)	341	40 (7.4)
Medicare Part D (Prescription drug coverage)	317	94 (16.6)
Medicare Advantage Plan (Medicare Managed Plans)	338	51 (9.3)
Military/CHAMPUS/TRICARE/VA health care program	340	50 (9.2)
All other insurance	387	31 (6.2)

missing. Otherwise, if only 1 or 2 were missing, then those items were assumed to not have any limitations (ie, 0 was added to the score).

RESULTS

We received 1122 survey responses. We excluded responses from those who were younger than 18 years, who did not live in the United States, who did not have EDS and were not a family member of someone with EDS, who had already completed the survey, or if any of these items were missing. A total of 174 responses were excluded via these criteria. We excluded duplicate responses ($n=38$) and responses that did not answer at least 2 items in each of the 3 sections of the survey ($n=26$).

The final analytic data set included 884 responses, of which 93% were completed by a person with EDS, 6% by a parent/guardian of a child with EDS, and 1% by a close family member. Parents/guardians and family members who completed the survey, including demographic information, did so on behalf of the person with EDS. Responses were received from individuals in all 50 states and the District of Columbia. Table 1 shows key demographic characteristics, EDS type, and year diagnosed; 84% reported having hypermobile EDS, and 30% reported being diagnosed in 2021-2022. It is possible that recently diagnosed patients tend to be more engaged in support groups and social media, and thus more likely to have completed the survey.

Appendix 1 (available online at <http://www.mcpiqjournal.org>) shows the results of the 27-item functional status measure for respondents who answered that they were completely unable or had significant limitations to complete the various activities. Respondents reported difficulty with physical household activities and social events and cognitive function. The median functional status score was 6 (IQR 3-10), indicating that 50% of respondents had at least 6 items with significant limitations or worse.

Financial Resources

With regards to individual and household income, we recommended that survey participants

refer to their 2022 tax return. More than 50% reported individual income less than \$25,000 and more than 30% reported household income less than \$50,000. Respondents received more financial assistance from their family and friends than from government sources. More than 80% of respondents had some type of commercial insurance; 29% reported receiving Medicaid in 2022. Table 2 reports individual and household income. Many participants reported receiving some type of financial assistance, including monetary assistance from family/friends (32.3%), Social Security Disability Insurance (16.0%), Supplemental Security Income disability benefits (6.6%), commercial disability insurance (6.6%), and monetary subsidies from charitable organizations or other assistance programs (5.1%). Appendix 2 (available online at <http://www.mcpiqjournal.org>) has a complete list of sources of financial assistance.

In 2022, 267 (31.7%) were employed full-time and 149 (17.7%) part-time. Appendix 3 (available online at <http://www.mcpiqjournal.org>) shows the complete employment status breakdown. Of the 536 who responded to the question, “did EDS play a major role in decision to move to part-time work or stop working?”, 82% said yes, 14% said no, and 5% were not sure. Table 3 reports insurance coverage, individual and/or family, for the year 2022.

Health Care Utilization and Spending

We asked about utilization of various types of health care services. Primary care physicians included family doctors, internists, pediatricians, and other providers of primary care. Specialty physicians included orthopedics, neurology, cardiology, gastroenterology, pain management, genetics, psychiatry, and other specialist providers. Examples of other therapy providers include massage, acupuncture, chiropractor, and manual therapy. Table 4 shows the median number of visits in 2022 for those reporting at least 1 visit. Of the 837 respondents reporting a primary care physician visit, the median was 5 visits in 2022, and the IQR, representing the middle 50% of values, was 3 to 10 visits. Specialty physician visits were greater: median, 12; IQR, 6 to 25 visits.

Table 5 shows the OOP health care spending by category. For each category, the number missing is reported, as well as the number of respondents who had those

TABLE 4. Utilization of Health Care Services, 2022

N=884	No. of missing	No. (%) of nonmissing	Median (IQR)
Primary care physicians	21	837 (97.0)	5 (3-10)
Specialty physicians	23	831 (96.5)	12 (6-25)
Physical therapy and occupational therapy visits	25	673 (78.3)	20 (10-40)
Other therapy providers	45	561 (66.9)	12 (5-28)
No. of emergency department visits	28	460 (53.7)	2 (1-4)
No. of hospital admissions	33	231 (27.1)	1 (1-2)
No. of operations	24	347 (40.3)	1 (1-2)
Median (IQR) reported for those with utilization for each item.			

expenses, with the percentage calculated for the subset that were not missing. Medians were reported for those with at least 1 expense.

Of the 838 who responded to the question, “Did the affected person receive the health care they needed”, 19% answered “no,” 51% answered “yes, sometimes,” and 30% said “yes, most of the time.”

DISCUSSION

Overall, the survey respondents reported high utilization of health care resources (primary care, specialty care, and physical and occupational therapy). This result reflects the multi-systems involvement of EDS. Our data analysis shows that EDS imposes significant financial burdens on patients.

Percentage of usage was highest for over-the-counter drugs, prescription medications, and supplements. The highest costs were associated with alternative or nontraditional treatments, mental health treatments, and oral operation and related care. Almost one-third of patients surveyed required financial assistance from family and friends. Additionally, patients require frequent consultations with primary care and specialists and need to undergo diagnostic evaluations and treatments for EDS-related complications. The total median OOP financial cost by our analysis was \$13,450 (IQR: \$6500-\$25,800). More than 50% of respondents were either employed or seeking work.

TABLE 5. Out-of-Pocket Health Care Spending

N=884	No. missing	No. (%) of nonmissing with expenses	Median \$ (IQR)
Direct medical expenses			
Health insurance premiums	152	541 (73.9)	3600 (1500-7000)
Health insurance deductibles	152	541 (73.9)	2000 (600-4500)
Copayments or coinsurance for physician office visits, emergency department visits, or hospital admissions	148	571 (77.6)	1000 (400-3000)
Prescription medication	105	702 (90.1)	600 (250-1500)
Diagnostic tests	176	479 (67.7)	600 (300-1700)
Genetic counseling or genetic tests	214	199 (29.7)	400 (225-800)
Alternative or nontraditional treatments	150	468 (63.8)	1000 (320-2290)
Mental health treatments	190	366 (52.7)	1000 (500-2400)
Physical/occupational/speech therapy	210	331 (49.1)	800 (350-1800)
Routine dental care	182	410 (58.4)	250 (110-500)
Routine eye care	192	430 (62.1)	250 (120-500)
Oral surgery, care, and services	232	147 (22.5)	1100 (600-2500)
Over-the-counter drugs	130	713 (94.6)	200 (100-480)
Medical foods	214	291 (43.4)	525 (300-2000)
Vitamins, calorie concentrates, and other supplements	139	670 (89.9)	400 (200-1000)
Specialty clothing	153	577 (78.9)	200 (100-400)
Equipment such as braces, collars, splints	137	593 (79.4)	200 (100-500)
Total direct expenses^a	257		12,100 (5400-21,600)
Other expenses			
Expenses related to purchasing equipment (such as pulse oximeter)	164	499 (69.3)	200 (100-500)
Purchasing/installing/modifying special equipment at home	236	147 (22.7)	150 (65-500)
Home modifications	243	54 (8.4)	725 (100-2,500)
Purchasing/installing/modifying a personal family vehicle	242	67 (10.4)	200 (60-3500)
Hiring someone for providing EDS-related daily care	237	89 (13.8)	1000 (300-3000)
Hiring someone to provide daily care to other household members due to affected person's reduced functional ability	244	70 (10.9)	1380 (500-5000)
Transportation costs related to medical care for EDS	192	459 (66.3)	600 (250-1850)
Travel-related expenses incurred because of EDS	254	203 (32.2)	500 (200-1200)
Total other expenses	263		650 (120-2500)
Total direct + other expenses	281		13,450 (6500-25,800)

Median (IQR) are reported for those who had any expenses for the item. For total direct and other expenses, respondents with ≥ 3 missing items (direct) and ≥ 2 missing item (indirect) were excluded. All other patients had at least 1 expense. Total direct + other expenses were calculated for those who met criteria for both direct and other expenses.

Strengths of our study include the sample size of 884 and a cross-section of demographic characteristics, including state of residence, insurance type, and income strata. Although we cannot state that our cohort is representative of the US population with EDS, individuals from all 50 states and the District of Columbia responded with a range of EDS diagnoses, including the rarer types. Ninety-five percentage of our study respondents were female. This is consistent with previous reports underscoring a bias toward White females.⁸⁻¹⁰ All insurance types were represented. The survey questionnaire was

modeled on the Everyday Life validated survey³ used to assess the economic burden of rare diseases. To minimize the survey burden and recall bias, we asked respondents to provide information about only 1 year's expenses (2022). To obtain accurate estimates of their expenses, we asked them to refer to income tax documents, explanation of benefits, and other bills and records.

Our study had some limitations. The sample population was self-selected and recruited through support groups, social media, and a few health care providers. Thus, the results may not be generalizable to those who do not

use social media, belong to support groups, or have computers. Another limitation of this type of survey was the amount of missing data. The study design did not include identifying participants in a way that we could followup and fill in missing responses. Missing data were predominately in the section where respondents reported their health care expenses and likely because participants needed to refer to their records and did not fully complete the survey.

Our study focused on the costs for 1 year (2022) and does not necessarily reflect the cumulative costs associated with living with EDS over time. There are no direct therapies or treatments approved for EDS; therefore, medical care is focused on symptom management. Because this management is lifelong, the associated costs are expected to accumulate over time and the long-term consequences are even more significant.

We did not measure reduced work productivity and the possible impact on retirement decisions. Although we measured functional status, we did not measure the impacts of chronic pain, fatigue, and vascular and musculoskeletal injuries that could have a financial impact and lead to reliance on disability and other types of financial assistance. Moreover, the emotional and psychologic stress associated with managing a lifelong condition can affect patients' overall well-being, potentially leading to additional health care costs for mental health services.^{11,12} These indirect costs, although less visible, significantly contribute to the overall burden of EDS. Even patients with insurance are vulnerable to financial burdens. Financial distress can cause patients to deplete their savings, borrow money, or use cost-coping strategies that lead to nonadherence to prescribed treatment.¹³ Additional research is needed to understand financial distress risk factors and suggest supportive care models for patients with substantial financial burdens.

More than half of the respondents were diagnosed in the past 5 years. We did not ask about time to diagnosis; however, it is known that patients with EDS often experience an extensive "diagnostic odyssey," resulting in significant delays in appropriate treatment, emotional stress, and economic loss.^{14,15}

CONCLUSION

Our study findings highlight the magnitude of the burden of health care spending on patients with EDS. The factors contributing to financial impact include both direct and indirect costs of accessing and receiving medical care.

POTENTIAL COMPETING INTERESTS

Dr Schubart reports grants from National Center for Advancing Translational Sciences, National Institutes of Health, through Grant UL1 TR002014 and Grant UL1 TR00045, from CTSI for the REDCap survey questionnaire data collection and storage, and from the Ehlers-Danlos Society (partial support) for the project in the amount of \$5000; reports institutional grants from Ehlers-Danlos Society (collaborator on various other unrelated Ehlers-Danlos Society projects) and Ehlers-Danlos Research Foundation (EDSRF; received funding on unrelated EDSRF research contracts); and reports leadership roles in the EDSRF. Dr Francomano reports institutional grants from Ehlers-Danlos Society projects (co-PI on various other unrelated projects) and EDSRF (Purdue University and Indiana University; co-PI on an unrelated grant); reports royalties as a Co-editor of the book "Symptomatic: The Symptom-Based Handbook for Ehlers-Danlos Syndromes and Hypermobility Spectrum Disorders (Elsevier, 2023)"; reports travel support for attending meetings from Ehlers-Danlos Society; is a consultant for WCG Clinical (Data Monitoring Committee); and is the Chair of Medical & Scientific Board of the Ehlers-Danlos Society; the Acting Chair of Medical Board of the EDSRF; and the Chair of Medical Board of the Alstrom Syndrome International. The other authors report no competing interests.

ETHICS STATEMENT

This research study was approved by the Pennsylvania State University Institutional Review Board, Human Research Protection Program (STUDY# 00022037, February 6, 2023). The research met the criteria for exempt research according to the policies of this institution and the provisions of applicable federal regulations.

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SUPPLEMENTAL ONLINE MATERIAL

Supplemental material can be found online at <http://www.mcpiqjournal.org>. Supplemental material attached to journal articles has not been edited, and the authors take responsibility for the accuracy of all data.

Abbreviations and Acronyms: **EDS**, Ehlers-Danlos syndrome; **OOP**, out-of-pocket

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