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Health Care Utilization and Costs Associated with Endometriosis Among Women with Medicaid Insurance

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ABSTRACT

BACKGROUND: Endometriosis is a painful chronic inflammatory disease caused by endometrial tissue implanting and growing outside the uterus, resulting in pelvic pain symptoms and subfertility. Treatment imposes a substantial economic burden on the patient and health care system.

OBJECTIVE: To evaluate direct health care utilization and costs among women newly diagnosed with endometriosis compared with age-matched controls in a U.S. Medicaid population.

METHODS: This retrospective cohort study used deidentified health care claims from the 2007-2015 MarketScan Multi-State Medicaid Database. Women (aged 18-49 years) newly diagnosed with endometriosis (ICD-9-CM 617.xx) during January 2008 through September 2014 were identified (date of first diagnosis = index date). Age-matched women without endometriosis (controls) were selected from the database and assigned index dates matching the distribution for endometriosis patients. Direct health care resource utilization (HCRU) and costs (medical and pharmacy) over the 12-month post-index period (2015 U.S. dollars) were computed by service category (hospitalization, emergency room visits, outpatient services, and prescriptions) and compared between study cohorts using the chi-square test for proportions and t-test for continuous variables.

RESULTS: The final sample included 15,615 endometriosis patients and 86,829 matched controls. HCRU during the 12-month post-index follow-up period was significantly higher for endometriosis cases compared with controls in all measured categories. Hospital admissions occurred among 33.1% of cases and 7.2% of controls, and 65.8% of endometriosis patients were admitted for endometriosis-related surgery. Emergency room visits occurred in 71.5% of cases, and 42.2% of controls. Mean (SD) office visits were 10.4 (8.5) for endometriosis patients and 5.1 (6.9) for controls. Endometriosis patients had significantly more prescription claims than controls, 45.9 (42.0) versus 25.1 (39.1). Mean total direct health care costs were \$13,670 (\$29,843) for cases versus \$5,779 (\$23,614) for controls. All differences between cases and controls were significant at $P < 0.001$.

CONCLUSIONS: Health care costs and resource utilization in all measured categories were higher among endometriosis cases than controls. The economic burden of endometriosis among patients with Medicaid insurance is substantial, underscoring the unmet medical need for earlier diagnosis and cost-effective treatments.

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What is already known about this subject

- Endometriosis is a chronic disease that is difficult to diagnose and treat, requiring significant expenditures of time and health care resources.
- Studies in commercially insured U.S. populations and multinational populations have documented the substantial economic and societal burden endured by women with endometriosis.

What this study adds

- This is the first study of the economic burden of endometriosis in the U.S. Medicaid population since 1995, reaching across multiple geographically distributed states (the 1995 study looked only at the California Medicaid population).
- Endometriosis patients receiving U.S. Medicaid coverage had significantly higher all-cause health care utilization and direct health care costs than controls, during pre-index and post-index periods, which was driven primarily by inpatient and outpatient medical costs (vs. pharmacy costs), with two thirds of endometriosis patients undergoing post-index endometriosis-related surgery, most commonly hysterectomy (40.2%).
- The economic burden of endometriosis for patients with Medicaid insurance is substantial.

Endometriosis is a chronic disease defined by implantation of extrauterine endometrial glandular tissue and stroma, commonly leading to inflammation and pelvic pain.¹⁻⁵ Recent prevalence estimates indicate 6%-10% of reproductive age women endure this condition, affecting more than 10 million women in the United States and nearly 200 million women worldwide.^{1,2,6-9}

Management involves pharmacologic and surgical interventions aimed at controlling symptoms by suppressing estrogen, reducing inflammatory processes, and limiting tissue damage.^{2,10,11} Medical management is the first-line approach to the treatment of endometriosis-related pain, whereas surgery is often used for initial or confirmatory diagnosis and for surgical removal of lesions, especially when medical treatments have failed.^{3,11-15}

Treatment can place a significant economic burden on the health care system and have resulting effects on society through productivity loss and reduced quality of life.^{4,16-18} The

annual economic burden of endometriosis, including direct health care costs and indirect productivity loss, was estimated to be \$22 billion in 2002 and \$69.4 billion in a 2009 follow-up study, a substantial apparent increase in costs attributed to endometriosis over time.^{19,20}

Although several earlier studies have reported the economic burden of endometriosis among commercially insured patients,^{16-18,21-23} little research has been published on the economic burden within the Medicaid population since 1995.²⁴ The objective of this study was to evaluate the economic burden in terms of health care resource utilization (HCRU) and direct health care costs among women newly diagnosed with endometriosis compared with age-matched controls in a U.S. Medicaid population.

Methods

Data Source

The study is based on administrative health care claims data from the 2007-2015 MarketScan Multi-State Medicaid Database, which contains the complete longitudinal records of inpatient services, outpatient services, prescription drug claims, long-term care, and other medical care for Medicaid-covered patients including dates of service, places of service, and all payments, pooled from approximately 12 geographically dispersed state Medicaid programs covering more than 6 million lives annually.

All database records are statistically deidentified and certified to be fully compliant with U.S. patient confidentiality requirements set forth in the Health Insurance Portability and Accountability Act (HIPAA) of 1996. Because this study used only deidentified patient records and did not involve the collection, use, or transmittal of individually identifiable data, institutional review board approval to conduct this study was not necessary.

Study Design

This study was a retrospective, observational U.S. claims database analysis of HCRU and costs incurred by female Medicaid patients newly diagnosed with endometriosis (cases) during the 12 months following initial endometriosis diagnosis, compared with a control population of age-matched females without an endometriosis diagnosis.

Study Population

Endometriosis cases included female patients with ≥ 1 nondiagnostic claim with a diagnosis of endometriosis (*International Classification of Diseases, Ninth Revision, Clinical Modification* [ICD-9-CM] diagnosis code 617.xx) in any position on a medical claim between January 1, 2008, and September 30, 2014 (patient selection period). Diagnostic claims, such as those for diagnostic radiology or laboratory tests, were not used for patient selection purposes. The index date was the first

endometriosis diagnosis claim date during the patient selection period. Patients were required to be between age 18 and 49 years on the index date and without an endometriosis diagnosis during the 12 months before the index diagnosis.

Controls included age-matched females without any endometriosis diagnosis between January 1, 2007, and September 30, 2015. The index date for control patients was randomly assigned during the patient selection period with a date distribution that matched the date distribution found among endometriosis patients.

Women in both case and control cohorts were required to have continuous Medicaid enrollment for 12 months before and after the index date. Women with evidence (diagnosis or procedure codes) of malignant neoplasms of female genitourinary organs (ICD-9-CM diagnosis codes 179.xx-184.xx); radical hysterectomy (see Appendix A for radical hysterectomy codes, available in online article); or for pregnancy and labor or delivery (see Appendix B for pregnancy and labor and delivery codes, available in online article) during the 12-month pre-index period were excluded.

Outcome Measures

All-cause and endometriosis-related HCRU and costs were evaluated for the 12-month pre- and post-index periods in total and by service categories including inpatient admissions; emergency room (ER) visits; physician office visits, specifically obstetrician/gynecologist (OB/GYN) visits; and outpatient prescriptions. Endometriosis-related HCRU and expenditures were defined by medical claims with a principal diagnosis of endometriosis; for endometriosis-related surgeries (laparotomy, laparoscopy, hysterectomy, oophorectomy, and other excision/ablation procedures); and by prescription claims for drugs potentially used in endometriosis management (danazol, goserelin, leuprolide, and nafarelin; oral, injectable, or intrauterine progestins; and estrogen/progestin oral contraceptives). Note that “endometriosis-related” surgeries and pharmaceutical treatments may arise for treatment of indications other than endometriosis or for contraception (for these subcategories, comparison of rates between cases and controls may be particularly important). All expenditures were the total paid (i.e., plan-paid plus patient-paid) amounts, adjusted to 2015 U.S. dollars using the medical care component of the Consumer Price Index.²⁵

Study Variables

Patient demographic variables measured on the index date included age, race, urban versus rural residence (based on metropolitan statistical area), and index year. Clinical characteristics were measured in the 12-month pre-index period. General health status was measured using the Deyo-Charlson Comorbidity Index (DCI), an aggregate measure of the patient's overall disease burden based on the weighted presence

of select diagnoses. Baseline presence of specific comorbidities was noted for abdominal/pelvic pain; acute coronary syndrome; anal/rectal pain; anxiety; asthma; bladder pain; chronic obstructive pulmonary disease (COPD); depression; diabetes; heart failure; hyperlipidemia; hypertension; irritable bowel syndrome; migraine; osteoarthritis; osteoporosis; pelvic peritoneal adhesions; upper respiratory infections; and gynecologic comorbid conditions (dysmenorrhea, dyspareunia, excessive menstruation, metrorrhagia, ovarian cysts, uterine fibroids, vaginitis, and claims for unspecified symptoms of the female genital organs). Prescription medications noted pre-index included opioids, nonsteroidal anti-inflammatory drugs (NSAIDs), antidepressants, and estrogen/progestin oral contraceptives.

Statistical Analysis

Dependent and independent variables were summarized descriptively, with categorical variables presented as the count and percentage of patients and continuous variables providing the number of observations, the mean, and standard deviation. Statistical tests of significance for observed differences between case and control groups were conducted using chi-square tests for categorical variables and t-tests for continuous variables. The threshold of statistical significance for all analyses was set a priori at 0.05. All data management, analytic file building, and statistical analyses were conducted using SAS software version 9.4 (SAS Institute, Cary, NC).

Multivariate analysis was used to compare cost outcomes in patients with and without endometriosis. Generalized linear models were used to estimate incremental costs for patients with endometriosis versus those without. The models used generalized estimating equations to account for within-patient correlation and used a gamma-distributed error and log link to account for the distributional characteristics of cost data. Estimation of the standard error of the marginal cost was conducted by using the delta method. All models controlled for differences between the 2 cohorts in the following patient characteristics: age; gender; geographic region; health plan type; DCI; and baseline comorbidities (acute coronary syndrome, anxiety, asthma, COPD, depression, diabetes, heart failure, hyperlipidemia, hypertension, irritable bowel syndrome, migraine, osteoarthritis, osteoporosis, upper respiratory infections, and uterine fibroids). The recycled prediction method was used to estimate the marginal or incremental costs associated with endometriosis. A P value of <0.05 was considered statistically significant.

Results

From this Medicaid population pool, a total of 15,615 endometriosis cases and 86,829 control patients met all selection criteria. Mean (standard deviation [SD]) age was 33.9 (7.3) years for cases and 34.0 (7.8) for controls. Matching on age occurred

TABLE 1 Baseline Demographic Characteristics of Study Patients

	Cases (n = 15,615)	Controls (n = 86,829)	P Value
Age, mean (SD)	33.9 (7.3)	34.0 (7.8)	0.030
Age group, years, n (%)			<0.001
18-24	1,552 (9.9)	9,890 (11.4)	
25-29	3,066 (19.6)	15,186 (17.5)	
30-34	3,930 (25.2)	20,295 (23.4)	
35-39	3,236 (20.7)	18,213 (21.0)	
40-44	2,399 (15.4)	14,500 (16.7)	
45-49	1,432 (9.2)	8,745 (10.1)	
Race, n (%)			<0.001
White	9,841 (63.0)	44,740 (51.5)	
Black	4,275 (27.4)	31,789 (36.6)	
Hispanic	316 (2.0)	2,173 (2.5)	
Other	1,183 (7.6)	8,127 (9.4)	
Medicaid eligibility, n (%)			<0.001
Disability	3,070 (19.7)	15,920 (18.3)	
Other	12,545 (80.3)	70,909 (81.7)	
Population density, n (%)			<0.001
Urban	10,466 (67.0)	63,001 (72.6)	
Rural	5,045 (32.3)	22,262 (25.6)	
Unknown	104 (0.7)	1,566 (1.8)	

SD = standard deviation.

before application of other inclusion criteria, which explains the small difference of about 8 weeks in the mean ages of the two groups. The case population had a lower proportion of black women with endometriosis than the control population (27.4% vs. 36.6% respectively) and a higher proportion of cases in rural areas (32.3% vs. 25.6%; Table 1).

Clinical Characteristics

Patients diagnosed with endometriosis generally had a higher comorbidity burden, with significantly higher mean (SD) DCI scores (cases 0.5 [1.0], controls 0.4 [1.0], P<0.001) measuring their overall chronic comorbidity burden and significantly greater baseline prevalence of all assessed specific comorbidities, especially abdominal/pelvic pain, upper respiratory infections, depression, anxiety, hypertension, and migraine compared with controls, all P<0.001. Furthermore, gynecologic conditions were far more prevalent pre-index in the endometriosis case cohort. Baseline opioid prescription claims were found for 77.2% of cases compared with 40.6% of controls, and the percentage of cases receiving prescriptions for NSAIDs, antidepressants, and oral contraceptives was nearly double that of the control population, all P<0.001 (Table 2).

Health Care Resource Utilization Outcomes

HCRU during the 12-month post-index follow-up period was significantly higher for endometriosis cases compared with

TABLE 2 Baseline Clinical Characteristics of Study Patients

	Cases		Controls		P Value
	(n = 15,615)	(n = 86,829)	(n = 86,829)	(n = 15,615)	
DCI, mean (SD)	0.49 (0.99)	0.35 (0.95)			<0.001
Comorbid conditions, n (%)^a					
Abdominal/pelvic pain	7,226 (46.3)	11,415 (13.1)			<0.001
Upper respiratory infections	5,867 (37.6)	18,508 (21.3)			<0.001
Depression	4,520 (28.9)	14,586 (16.8)			<0.001
Anxiety	4,381 (28.1)	12,266 (14.1)			<0.001
Hypertension	3,232 (20.7)	12,432 (14.3)			<0.001
Migraine	2,393 (15.3)	5,360 (6.2)			<0.001
Asthma	1,944 (12.4)	7,051 (8.1)			<0.001
COPD	1,537 (9.8)	5,165 (5.9)			<0.001
Hyperlipidemia	1,464 (9.4)	6,099 (7.0)			<0.001
Diabetes	1,426 (9.1)	6,506 (7.5)			<0.001
Osteoarthritis	887 (5.7)	3,129 (3.6)			<0.001
Gynecologic conditions, n (%)^a					
Any gynecologic condition	11,819 (75.7)	13,852 (16.0)			<0.001
Unspecified gynecologic symptoms	6,840 (43.8)	3,908 (4.5)			<0.001
Excessive/frequent menstruation	3,969 (25.4)	2,752 (3.2)			<0.001
Ovarian cysts	3,471 (22.2)	2,032 (2.3)			<0.001
Dysmenorrhea	2,955 (18.9)	1,722 (2.0)			<0.001
Vaginitis	2,816 (18.0)	6,779 (7.8)			<0.001
Uterine fibroids	2,230 (14.3)	1,159 (1.3)			<0.001
Dyspareunia	1,289 (8.3)	515 (0.6)			<0.001
Medication use, n (%)					
Opioids	12,062 (77.2)	35,236 (40.6)			<0.001
NSAIDs	9,511 (60.9)	28,578 (32.9)			<0.001
Antidepressants	7,452 (47.7)	23,960 (27.6)			<0.001
Estrogen/progestin oral contraceptives	3,205 (20.5)	9,794 (11.3)			<0.001
Pre-index utilization and expenditures					
Patients with an admission, n (%)	1,822 (11.7)	6,187 (7.1)			<0.001
Patients with an emergency room visit, n (%)	11,124 (71.2)	36,939 (42.5)			<0.001
Physician office visits per patient, mean (SD)	10.36 (8.15)	4.98 (6.49)			<0.001
Prescriptions claims per patient, mean (SD)	39.2 (38.8)	23.6 (37.0)			<0.001
Total health care costs, \$, mean (SD)	8,160 (19,913)	5,537 (21,568)			<0.001

^aOnly comorbidities with >5% occurrence in either cohort are listed. COPD=chronic obstructive pulmonary disease; DCI=Deyo-Charlson Comorbidity Index; NSAIDs=nonsteroidal anti-inflammatory drugs; SD=standard deviation.

TABLE 3 Health Care Resource Utilization

	Cases	Controls	P Value
	(n = 15,615)	(n = 86,829)	
All-cause health care utilization			
Patients with an admission, n (%)	5,168 (33.1)	6,219 (7.2)	<0.001
Admissions per patient, mean (SD)	0.48 (0.97)	0.12 (0.63)	<0.001
Length of stay per admission, mean (SD)	1.30 (2.54)	0.39 (2.05)	<0.001
Patients with an emergency room visit, n (%)	11,164 (71.5)	36,624 (42.2)	<0.001
Emergency room visits per patient, mean (SD)	3.24 (5.58)	1.24 (2.79)	<0.001
Patients with a physician office visit, n (%)	15,121 (96.8)	62,194 (71.6)	<0.001
Physician office visits per patient, mean (SD)	10.44 (8.50)	5.10 (6.90)	<0.001
Patients with an OB/GYN visit, n (%)	4,443 (28.5)	7,097 (8.2)	<0.001
OB/GYN visits per patient, mean (SD)	0.85 (1.84)	0.16 (0.69)	<0.001
Patients with a prescription claim, n (%)	15,492 (99.2)	65,685 (75.6)	<0.001
Endometriosis-related health care utilization			
Patients with an admission, n (%)	2,257 (14.5)	N/A	<0.001
Admissions per patient, mean (SD)	0.15 (0.37)	N/A	<0.001
Length of stay per admission, mean (SD)	0.52 (1.77)	N/A	<0.001
Patients with an emergency room visit, n (%)	1,738 (11.1)	N/A	<0.001
Emergency room visits per patient, mean (SD)	0.15 (0.56)	N/A	<0.001
Patients with a physician office visit, n (%)	7,123 (45.6)	N/A	<0.001
Physician office visits per patient, mean (SD)	0.90 (1.53)	N/A	<0.001
Patients with an OB/GYN visit, n (%)	2,259 (14.5)	N/A	<0.001
OB/GYN visits per patient, mean (SD)	0.26 (0.80)	N/A	<0.001
Patients with endometriosis-related prescription claim, ^a n (%)	4,721 (30.2)	12,903 (14.9)	<0.001
Prescription claims per patient, mean (SD)	1.32 (2.92)	0.79 (2.50)	<0.001
Patients with endometriosis-related surgery, ^a n (%)	10,275 (65.8)	989 (1.1)	<0.001
Laparotomy	420 (2.7)	60 (0.1)	<0.001
Laparoscopy ^b	4,913 (31.5)	552 (0.6)	<0.001
Hysterectomy	6,278 (40.2)	418 (0.5)	<0.001
Hysterectomy with same-day oophorectomy	293 (1.9)	7 (0.01)	<0.001
Oophorectomy	610 (3.9)	32 (0.04)	<0.001
Other excision/ablation	68 (0.4)	10 (0.01)	<0.001

^a“Endometriosis-related” prescription-claims and surgeries are defined solely by drug and surgery types and may not specifically indicate use for endometriosis. ^bDoes not include laparoscopic hysterectomy or laparoscopic oophorectomy, which are included under their corresponding surgery categories. N/A=not applicable; OB/GYN=obstetrician/gynecologist; SD=standard deviation.

controls in all measured categories (Table 3). All-cause hospital admissions occurred for 33.1% of cases and 7.2% of controls, with significantly longer mean (SD) lengths of stay for cases at 1.30 (2.54) days versus 0.39 (2.05) days for controls. With 71.5% of cases and 42.2% of controls having an ER visit, the mean number of ER visits per patient with endometriosis was

TABLE 4 Medication Utilization Among Patients with Endometriosis, Pre- and Post-Index

	Pre-Index	Post-Index
	(N = 15,615)	
Endometriosis medication utilization, n (%)		
Oral contraceptives (combined estrogen and progestin)	3,205 (20.5)	2,536 (16.2)
Progestins only	2,635 (16.9)	1,910 (12.2)
Gonadotropin-releasing hormone (GnRH) agonists	379 (2.4)	1,249 (8.0)
Danazol (synthetic derivative of testosterone)	0 (0.0)	0 (0.0)

more than double that of controls (3.24 [5.58] versus 1.24 [2.79], respectively). Mean all-cause office visits per endometriosis patient (10.4 [8.5]) were similarly twice that of controls (5.1 [6.9]). Most patients in both cohorts had at least 1 prescription claim; however, endometriosis patients had significantly more prescription claims over the 12-month follow-up than controls (45.9 [42.0] vs. 25.1 [39.1], respectively). All differences were highly significant at $P < 0.001$.

Endometriosis-related health care utilization was also tracked with 14.5% of cases having an endometriosis-related hospital admission, 11.1% having an endometriosis-related ER visit, and 45.6% having an endometriosis-related physician office visit (Table 3). Notably, 65.8% of endometriosis patients had an endometriosis-related surgery, including 40.2% with hysterectomy and 31.5% for laparoscopy. Claims for prescription medications used for disease management were common both pre- and post-index; however, with the exception of gonadotropin-releasing hormone agonists, their use decreased in the post-index period (Table 4).

Direct Expenditure Outcomes

Patients with endometriosis showed overall significantly higher direct all-cause health care costs compared with those without endometriosis, with mean (SD) total health care costs of \$13,670 (\$29,843) versus \$5,779 (\$23,614) for controls during the 12-month post-index follow-up periods. The highest expenditure category for endometriosis patients was inpatient admissions (\$5,785) followed by other outpatient services (\$4,363) and outpatient prescriptions (\$2,096). Costs classified as endometriosis-related comprise 22.4% of total costs, or \$3,069 (\$11,795), with a mean of \$212 (\$941) attributable to endometriosis-relevant pharmacotherapy. All differences between cases and controls were highly significant at $P < 0.001$ (Table 5).

Adjusted Health Care Expenditures

Results from the multivariable analysis indicated that, adjusted for baseline demographic and clinical characteristics, patients

TABLE 5 Direct Health Care Expenditures, 12 Months Post-Index

	Cases	Controls	P Value
	(n = 15,615)	(n = 86,829)	
All-cause health care costs, \$, mean (SD)			
Total health care costs	13,670 (29,843)	5,780 (23,614)	<0.001
Inpatient admissions	5,785 (25,550)	1,689 (17,842)	<0.001
Emergency room	819 (1,985)	270 (914)	<0.001
Physician office visits	606 (675)	277 (592)	<0.001
OB/GYN visits	60 (138)	12 (53)	<0.001
Outpatient pharmacy	2,096 (6,173)	1,281 (5,140)	<0.001
Endometriosis-related costs, \$, mean (SD)			
Total health care costs	3,069 (11,795)	30 (145)	<0.001
Inpatient admissions	1,629 (11,563)	0 (0)	<0.001
Emergency room	43 (224)	0 (0)	<0.001
Physician office visits	48 (99)	0 (0)	<0.001
OB/GYN visits	19 (59)	0 (0)	<0.001
Outpatient pharmacy	212 (941)	30 (145)	<0.001

OB/GYN = obstetrician/gynecologist; SD = standard deviation.

with endometriosis showed a significantly higher burden when compared with those without endometriosis, with mean total annual health care expenditures of \$11,686 (\$20,356) versus \$5,216 (\$9,086) in the year following diagnosis, for a mean annual incremental health care cost of endometriosis estimated at \$6,470 ($P < 0.0001$).

Discussion

This Medicaid population study found HCRU and expenditures were significantly higher among endometriosis cases than controls in all measured categories, with total expenditures for cases more than double that of controls in both the unadjusted and multivariate-adjusted cost estimates, largely driven by the cost of hospitalizations. These results in a multistate Medicaid population are similar in many ways to the findings of previous studies in commercially insured populations and those using systematic literature reviews, particularly in finding significantly higher HCRU and expenditures for endometriosis patients driven by hospitalizations.^{16-19,20,22,23}

Our study analyzed HCRU and costs within the 12-month post-index period, in concordance with the existing body of literature consistently reporting HCRU and costs were highest in the first year after endometriosis diagnosis.^{16,21-23} Mean total all-cause health care costs during the first post-index year were similar between the current Medicaid study (endometriosis cases \$13,670, controls \$5,780) and the U.S.-based commercially insured population studies in which average costs for endometriosis cases ranged \$12,118 to \$16,573 compared with controls ranging \$3,747 to \$7,428 (adjusted to 2015 U.S. dollars).^{16-18,22,23}

Total direct all-cause costs for endometriosis patients were driven largely by medical costs, led by hospitalizations (42.3%

of costs) and outpatient services (including office visits; 36.4%), with outpatient prescriptions at 15.3% of the total. Other studies using commercially insured patient data showed similar percentages of the total paid for inpatient admissions (Mirkin et al., 2007, 43.8%; Fuldeore et al., 2015, 37.2%).^{16,22} Pharmacy costs for the Medicaid patients were a slightly higher percentage of the total than other commercial-based studies that ranged from 9% to 11%.^{16,22,23} Although ER visits were 6.0% of total costs, it is notable that 71.5% of Medicaid cases reported an ER visit during follow-up, which is dramatically higher than the commercially insured cohorts that ranged from 26% to 33%.

In this Medicaid-insured population, endometriosis patients had significantly higher all-cause HCRU and expenditures than controls during both pre- and post-index periods, although post-index HCRU and costs for endometriosis patients were all much higher than pre-index (except for ER visits). Endometriosis patients had significantly higher pre-index comorbidity scores (mean DCI 0.49 for cases, 0.35 for controls, $P < 0.001$) and higher prevalence of all reported comorbidities. The high pre-index HCRU and costs found for endometriosis patients may be sequelae of fulminant symptoms present with delayed diagnoses. This hypothesis is supported by the high use of oral contraceptives in the pre-index period (20.5% for cases, 11.3% for controls, $P < 0.001$), which decreases to 16.2% among cases in the post-index period. Hormonal medication is often employed as a low-risk, empirical treatment when endometriosis is suspected before a definitive diagnosis by laparoscopy.³ Such hormonal treatment would then become unnecessary after formal diagnosis and surgical intervention.

High pre-index use of opioids was also observed among endometriosis patients (77.2% for cases, 40.6% for controls, $P < 0.001$) and may be an indicator of endometriosis-related chronic pain management or management of secondary acute pain from the reduced conditioned pain modulation that often accompanies chronic pain.^{26,27} Given the risk of dependency and abuse,²⁸ there is need for further investigation into opioid treatment patterns in this population with a specific focus on changes after diagnosis and treatment for the underlying condition.

The recent study by Fuldeore et al., which spanned 2000-2010, reported that 40% of endometriosis patients were hospitalized for any cause during the first year following diagnosis.²² The current analysis spanning 2007-2015 found 33.1% of endometriosis patients with an all-cause admission. With surgical treatment reported to be common within the first year of diagnosis, this may represent a decrease in inpatient admissions for treating endometriosis.^{17,21} However, our data also show that 65.8% of cases received endometriosis-related surgery, whether inpatient or outpatient. Surgery thus appears to remain a mainstay of endometriosis therapy for Medicaid patients in our analysis, with surgeries appearing to shift from the inpatient into the outpatient arena. Despite advances in

medical therapy, 40.2% of Medicaid cases underwent hysterectomy, which remains the most common surgery during the first year following diagnosis.

Limitations

Administrative health care claims are very valuable for studying health care utilization and costs; however, analyses are limited by the claims data available and limited to the time frame of the study. Potential exists for misclassification of cases and controls, as symptomatic women may have inadvertently been included in the control group in the absence of a recorded endometriosis diagnosis during the study time frame. We can also not be 100% certain that every endometriosis patient is a newly diagnosed patient; it is possible that identified endometriosis patients who had a diagnosis of endometriosis at least 12 months before their assigned index date, without intervening evidence for endometriosis, are included in our sample.

Medicines and disease management not covered by Medicaid are missing from this analysis, including over-the-counter pain and other medications (e.g., NSAIDs and naturopathic remedies), noncovered providers, or other self-management techniques. Clinical details such as severity of illness and other sociodemographic variable found in patient charts or medical records (e.g., endometriosis-related symptoms and patient assessments such as height, weight, and smoking status) were unavailable for examining the influence of these factors on treatment choices and outcomes. Specifically, although we used multivariate modeling to control for differences in baseline characteristics when estimating the marginal cost of disease, many of the aforementioned unavailable clinical and demographic details may influence health care costs and could not be controlled for. Therefore, the calculated marginal cost of endometriosis may be over or underestimated.

Opioid use included all types, strengths, and dosage forms. Given the frequency of observed use, additional research is warranted to better classify opioid use.

Finally, the data source for this study is a convenience sample of contributing Medicaid payers, and although composed of data from multiple states, it does not constitute a random selection of the total U.S. Medicaid population, so findings may not be generalizable to women with endometriosis who are covered by other U.S. health insurers or who are uninsured.

Conclusions

Medicaid patients with a diagnosis of endometriosis had significantly higher health care resource utilization and costs across all categories than age-matched controls without a diagnosis of endometriosis. Increased hospitalizations were the primary driver of higher health care costs among endometriosis patients. These findings confirm previous studies of commercially insured patients and underscore the continued unmet need for early diagnosis and treatment of endometriosis.

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DISCLOSURES

This study was funded by AbbVie and conducted by Truven Health Analytics, an IBM Company. AbbVie participated in developing the study design, data analysis and interpretation, manuscript writing and revisions, and approval for publication. Soliman and Vora are employees of AbbVie and may own AbbVie stock/stock options. Surrey has served in a consulting role on research to AbbVie and is on the speaker bureau for Ferring Laboratories. Bonafede and Nelson are employees of Truven Health Analytics, an IBM Company, which received compensation from AbbVie for the overall conduct of the study and preparation of the manuscript. Agarwal has served in a consulting role on research to AbbVie.

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Health Care Utilization and Costs Associated with Endometriosis Among Women with Medicaid Insurance

APPENDIX A Coding Used to Identify Radical Hysterectomy Procedures

Code Type	Code	Description
ICD-9-CM PROCEDURE	68.6	Radical abdominal hysterectomy
ICD-9-CM PROCEDURE	68.61	Laparoscopic radical abdominal hysterectomy
ICD-9-CM PROCEDURE	68.69	Other and unspecified radical abdominal hysterectomy
ICD-9-CM PROCEDURE	68.7	Radical vaginal hysterectomy
ICD-9-CM PROCEDURE	68.71	Laparoscopic radical vaginal hysterectomy
ICD-9-CM PROCEDURE	68.79	Other and unspecified radical vaginal hysterectomy
ICD-9-CM PROCEDURE	68.8	Pelvic evisceration
CPT-4	58210	
CPT-4	58240	
CPT-4	58285	
CPT-4	58548	

CPT-4 = Current Procedural Terminology, 4th Edition; ICD-9-CM = International Classification of Diseases, Ninth Revision, Clinical Modification.

APPENDIX B Coding Used to Identify Pregnancy, Labor, and Delivery

Code Type	Code	Description
ICD-9-CM PROCEDURE	72.xx-75.xx	Obstetric procedures
ICD-9-CM PROCEDURE	69.01	Curettage of uterus for termination of pregnancy or after delivery/abortion
ICD-9-CM PROCEDURE	69.02	Curettage of uterus for termination of pregnancy or after delivery/abortion
ICD-9-CM PROCEDURE	69.51	Curettage of uterus for termination of pregnancy or after delivery/abortion
ICD-9-CM PROCEDURE	69.52	Curettage of uterus for termination of pregnancy or after delivery/abortion
CPT	01960-01963	Anesthesia during delivery
CPT	01967-01969	Anesthesia during delivery
CPT	59000-59899	Maternal care and delivery
CPT	76801-76828	Fetal ultrasound
CPT	83661-83664	Fetal lung maturity assessment
CPT	76941	Ultrasound guidance for pregnancy-related procedures
CPT	76945	Ultrasound guidance for pregnancy-related procedures
CPT	76946	Ultrasound guidance for pregnancy-related procedures
CPT	80055	Additional pregnancy-related procedures
CPT	82105	Additional pregnancy-related procedures
CPT	82106	Additional pregnancy-related procedures
CPT	82143	Additional pregnancy-related procedures
CPT	87231	Additional pregnancy-related procedures
CPT	83632	Additional pregnancy-related procedures
CPT	84163	Additional pregnancy-related procedures
CPT	84702	Additional pregnancy-related procedures
CPT	88235	Additional pregnancy-related procedures
CPT	88267	Additional pregnancy-related procedures
CPT	88269	Additional pregnancy-related procedures
CPT	99436	Additional pregnancy-related procedures
CPT	8801x	Infant/newborn necropsy
CPT	88028	Infant/newborn necropsy
CPT	88029	Infant/newborn necropsy
CPT	S2227	Abortion
CPT	S2262	Abortion
CPT	S2265	Abortion
CPT	S2266	Abortion
CPT	S2267	Abortion

CPT-4 = Current Procedural Terminology, 4th Edition; ICD-9-CM = International Classification of Diseases, Ninth Revision, Clinical Modification.