Heavy Menstrual Bleeding Treatment Patterns and Associated Health Care Utilization and Costs

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ABSTRACT

- *Objective:* To evaluate health care resource utilization and costs associated with heavy menstrual bleeding (HMB) treatment and to compare outcomes between patients without an identified underlying condition (idiopathic HMB) and patients with an identified cause (organic HMB).
- *Design:* Retrospective claims analysis.
- *Participants:* Commercially insured female enrollees aged 18-49 years with newly diagnosed HMB.
- *Measurements:* The index date was the first claim date with an HMB diagnosis; patients were followed from 6 months prior to index date (pre-index period) to 18 months following index date (post-index period). Treatment patterns, health care resource utilization, and cost outcomes were evaluated post-index and stratified by cohort and age-group. Variables were descriptively analyzed with comparisons across cohorts.
- *Results:* Newly diagnosed HMB patients (n = 34,941; mean age 40.5 years) included 21,362 idiopathic and 13,579 organic HMB patients. Among idiopathic HMB patients, over 30% did not receive any evaluated treatments; 68.8% received at least 1 treatment episode (57.6% received only 1 treatment episode and 10.9% only 2). More than half (55.7%) underwent surgery as their initial treatment. Among single-episode treatments, hysterectomy was associated with the highest HMB-related costs for both cohorts (idiopathic: mean $9089 [SD $5940], median $8493; organic: mean $9395 [SD $6291], median $8634). GLM analysis revealed predicted HMB-related costs of $3858.59 for the idiopathic cohort and $5788.64 for the organic cohort.
- *Conclusions:* HMB is associated with increased health care resource utilization and costs.

Heavy menstrual bleeding (HMB), characterized by excessive menstrual blood loss and cramping that interferes with usual daily activities [1], can have a significantly adverse impact on premenopausal women's quality of life [2] and can cause health issues such as anemia and fatigue [3]. In clinical trials, HMB has been defined as a mean menstrual blood loss ≥ 80 mL per cycle [4]. However, HMB diagnosis and treatment are usually based on patient self assessment [5,6].

Among reproductive-age women, prevalence rates of HMB range from 10% to 30% [7]. Of women who seek consultations for HMB associated with menses that occur at predictable intervals, half have some uterine abnormality or organic pathology. The pathologic cause among younger women (< 40 years of age) is most often fibroids, whereas endometrial polyps are more frequent among women over 40 [8]. It is important to note that endocrine conditions, such as polycystic ovary syndrome (PCOS) and thyroid disorders, are more likely to be associated with irregular menses, with or without heavy bleeding [9]. Most recently Lethaby et al estimated that up to 80% of women who are treated for HMB have no anatomical pathology and are considered to have idiopathic HMB [8,10].

Both medical treatments and surgical interventions are available to treat HMB [6]. Four prescription medications are FDA-approved for the treatment of HMB: levonorgestrel-releasing intrauterine system (LNG-IUS), tranexamic acid, oral medroxyprogesterone acetate,

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and norethindrone [11]. Nonsteroidal anti-inflammatory drugs (NSAIDs), danazol, and depot goserelin (a gonadotropin-releasing hormone antagonist) are also commonly used [12]. Surgical treatments include myomectomy, uterine artery embolization (UAE), endometrial ablation, and hysterectomy [11]. Both myomectomy and UAE are fertility-sparing procedures, although pregnancy is not recommended post-UAE. In comparison, patients receiving UAE procedures report greater symptom improvement, whereas patients receiving myomectomies frequently require additional surgical interventions [13]. While hysterectomy is 100% effective in eliminating menstrual bleeding, it is generally the most costly option and can be associated with significant complications [10]. Endometrial ablation is less invasive than hysterectomy and preserves the uterus, but repeat procedures are sometimes required and the patient also needs some form of contraception if sexually active; therefore, ablation can be as costly as hysterectomy [14].

HMB is also associated with significant economic burden. Liu and colleagues (2007) [7] reported that the estimated annual direct and indirect economic costs of HMB were approximately $1 billion and $12 billion, respectively. A representative survey of 2805 American women conducted in 2002 estimated the indirect costs associated with HMB (ie, work loss) to be $1692 annually per woman with HMB. Moreover, women who have heavier menstrual flows were only 72% as likely to be working as were women who have a lighter or normal flow (odds ratio [OR] 0.72, 95% confidence interval [CI] 0.56, 0.92) [15].

Most studies evaluating the burden of HMB have assessed overall direct costs to the healthcare system or the comparative cost-effectiveness of specific treatments, but the expenditures associated with specific types of resource utilization among women with HMB have not been well studied. The objectives of this study were to assess healthcare resource utilization and costs associated with the treatment of patients with HMB and compare these outcomes between patients with an identified underlying condition (the organic HMB cohort) and those without an identified underlying condition (the idiopathic HMB cohort).

METHODS

Study Design and Data Source

We conducted a retrospective analysis of medical and pharmacy claims data from a large US managed care database during the period 1 July 2003 to 31 August 31 2009. Roughly 13 million individuals with full medical and pharmacy benefit coverage were enrolled in the plan in 2009. These enrollees were from across the United States, with heaviest representation in the South (50%) and Midwest (30%).

No identifiable protected health information was extracted or accessed during the course of the study pursuant to the Health Insurance and Portability and Accountability Act (HIPAA) of 1996 [16]. The use of de-identified data does not require a separate institutional review board approval or waiver of authorization.

Patient Inclusion and Exclusion Criteria

Commercially-insured enrollees diagnosed with HMB as indicated by the presence of at least 1 medical claim with an *International Classification of Diseases, 9th Revision, Clinical Modification* (ICD-9-CM) diagnosis code of 626.2 ("excessive or frequent menstruation") or 627.0 ("premenopausal menorrhagia") in the primary diagnosis position during the period 1 January 2004 to 29 February 2008 (identification period) were included in the study (**Figure**). After a 6-month pre-index period, the date of the first claim with a diagnosis of HMB was considered the index date. Other inclusion criteria included 18 to 49 years of age as of the year of the index date, having a second medical claim with a diagnosis of HMB in the primary position within 180 days of the index date, and having been continuously enrolled with pharmacy and medical benefits for 6 months prior to the index date (pre-index period) and 18 months following the index date (post-index period).

Patients were excluded from the study if they had at least 1 medical claim with a diagnosis for HMB (ICD-9-CM 626.2 or 627.0) in any position during the pre-index period, or diagnosis of any of the following at any time and in any position throughout the study period (codes available from author): cervical dysplasia, cancer, endometrial hyperplasia with atypia, or endometrial intraepithelial neoplasia. In addition, patients who had undergone hysterectomy or endometrial ablation (codes available from author) during the pre-index period were excluded from the study.

Cohort Assignment and Observational Period

Patients were assigned to 1 of the 2 study cohorts based on whether an underlying cause of HMB was identified during the pre-index period through 60 days following the index date. Women with an identifiable underlying cause of HMB such as uterine fibroids (ICD-9-CM code

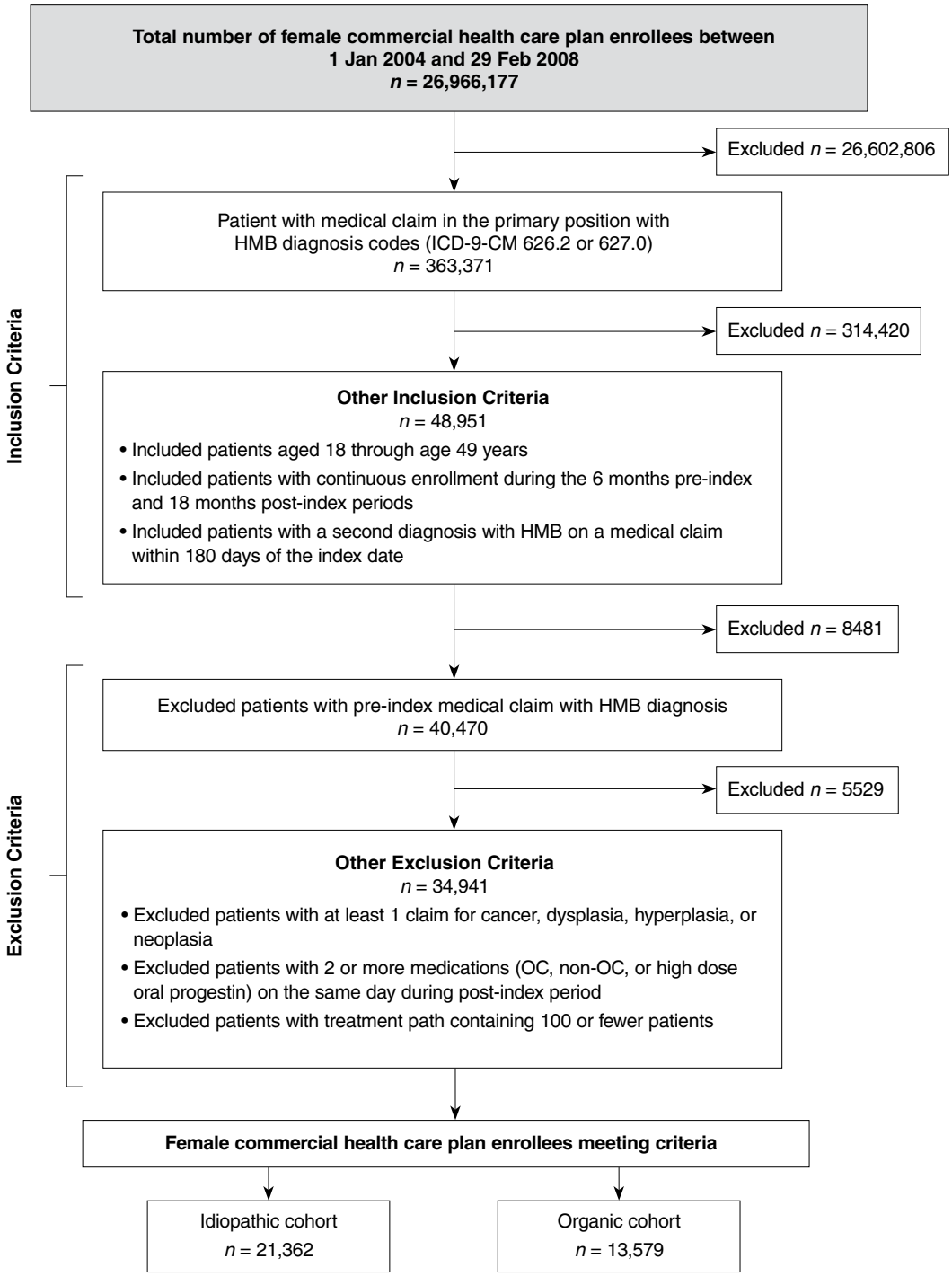

Figure. Inclusion/exclusion criteria flow diagram. HMB = heavy menstrual bleeding; ICD-9-CM = International Classification of Diseases, 9th Revision, Clinical Modification diagnosis codes; OC = oral contraceptives.

218.x), cervical or endometrial polyps (ICD-9-CM codes 622.7, 621.0), benign uterine neoplasm (ICD-9-CM code 219.x), simple endometrial hyperplasia (ICD-9-CM code 621.31), or bleeding disorders (see Appendix C), were assigned to the organic cohort. Women with no underlying conditions identified as causing HMB during the same period were assigned to the idiopathic cohort. Women who received a diagnosis associated with an endocrine disorder (eg, ICD-9-CM code 256.4 polycystic ovaries) were not included in this study, as these would generally present with both heavy and irregular menstrual bleeding, instead of one of the diagnostic codes assigned for HMB. Women could be assigned to only one cohort throughout the study period, regardless of any diagnosis assigned beyond the period defined above.

During the 6-month pre-index period, subjects' baseline demographic and clinical characteristics were assessed. All-cause and HMB-related healthcare resource utilization and cost outcomes were evaluated during the 18-month post-index period, inclusive of the index date. Resource utilization was calculated for physician office visits, outpatient facility visits, emergency department (ED) visits, and inpatient admissions, and "HMB-related" was defined by the presence of claims with primary or secondary diagnosis codes ICD-9-CM 626.2 or 627.0. Healthcare costs were computed as the combined amounts paid by the health plan and by patients, and healthcare costs were categorized as total, medical, pharmacy, ambulatory (office and outpatient), emergency services, inpatient, and other costs. All healthcare costs were adjusted using the annual medical care component of the Consumer Price Index (CPI) to reflect inflation between the start of the study period and 2010.

Study Measures

Demographic characteristics were determined from enrollment data and medical and pharmacy claims and included age, age-group (18–34, 35–39, 40–49 years), and geographic region of enrollment. The age-groups were based on clinical differences at age 35 and above 40 which may influence treatment patterns and associated costs. Clinical characteristics, derived uniquely from the database, such as Quan-Charlson comorbidity score [17,18] and the most common comorbid conditions during pre-index were analyzed. Treatment patterns in this population have been previously presented [19].

HMB-related medical treatments and surgical procedures administered to patients during the post-index period were collected. Medical treatments identified for evaluation were categorized as: oral contraceptives (OC; progestin only or combination estrogen/progestin), non-OC (including intrauterine device [IUD], contraceptive patch, implants, injectables, vaginal ring), and high-dose oral progestins (norethindrone acetate and medroxyprogesterone acetate). Of note, tranexamic acid was not available during the study period and over-the-counter medications are not captured in claims data. Surgical procedures of interest were endometrial ablation, myomectomy, uterine artery embolization, and hysterectomy.

Rates and costs of no treatment, single-episode treatments and multiple-episode treatment paths were assessed and stratified by cohort and by age-group.

Statistical Analyses

All study variables, including baseline and outcome measures, were analyzed descriptively. Comparisons were made across cohorts. A P value of ≤ 0.05 was considered statistical significance. The difference between unadjusted mean values of continuous variables was evaluated using t tests, and chi-square tests were conducted to evaluate unadjusted differences in proportions. A generalized linear modeling (GLM) analysis was performed to determine the relationship between cohort membership and post-index HMB-related costs. Analyses were performed using SAS®, Version 9 (SAS Institute, Cary, NC) and Stata®, Version 9 (StataCorp, College Station, TX).

RESULTS

Demographic and Clinical Characteristics

Our analysis identified 34,941 women newly diagnosed with HMB (Figure) with 13,579 in the organic HMB cohort and 21,362 in the idiopathic HMB cohort. The mean age for the total study sample was 40.5 years, while the mean age of the organic cohort and idiopathic cohort was 42.3 and 39.4 years, respectively (**Table 1**). Overall, there were more women in the 35 and over age-groups than in the younger than 35 age-group. There were 73.9% of women with organic HMB and 55.9% of women with idiopathic HMB who were over the age of 40 years. 80% of the women were located in the Midwest or South regions, which is consistent for patients derived from this commercially insured population.

Treatment Patterns

A brief summary of HMB treatment patterns in this population follows [19]. For women with organic HMB

Table 1. Demographic and Clinical Characteristics of Patient Sample, Overall and by Cohort

Demographic/ Clinical Characteristics	Total (*n* = 34,941)		Idiopathic (*n* = 21,362)		Organic (*n* = 13,579)		
	Mean	**SD**	**Mean**	**SD**	**Mean**	**SD**	***P* Value**
Age (years)	40.5	6.3	39.4	6.8	42.3	5.1	< 0.001
Charlson Comorbidity Score	0.1	0.4	0.1	0.4	0.2	0.5	< 0.001
	n	**%**	***n***	**%**	***n***	**%**	***P* Value**
Age-group							
18-34 years	3651	16.2	4537	21.2	1114	8.2	< 0.001
35-39 years	7313	20.9	4878	22.8	2435	17.9	
40-49 years	21,977	62.9	11,947	55.9	10,030	73.9	
Geographic region							
Northeast	2564	7.3	1559	7.3	1005	7.4	< 0.001
Midwest	10,351	29.6	6442	30.2	3909	28.8	
South	17,484	50.0	10,516	49.2	6968	51.3	
West	4542	13.0	2845	13.3	1697	12.5	

Pre-Index All-Cause Health Care Utilization and Costs by Cohort	Idiopathic (*n* = 21,362)			Organic (*n* = 13,579)			
	Mean	**SD**	**Median**	**Mean**	**SD**	**Median**	***P* Value**
Health care utilization							
Physician office visits	4.4	5.6	3.0	4.6	5.4	3.0	< 0.001
Outpatient visits	1.2	2.4	0.0	1.4	2.6	0.0	< 0.001
Inpatient admissions	0.0	0.2	0.0	0.0	0.2	0.0	0.056
Emergency department visits	0.4	1.7	0.0	0.4	1.7	0.0	0.840
Medical costs							
Physician office visits	601	1135	289	655	1072	344	< 0.001
Outpatient visits	647	2538	0	730	2864	0	0.006
Inpatient admissions	332	2976	0	336	3365	0	0.905
Emergency department visits	64	274	0	65	284	0	0.581
Pharmacy costs	477	1048	150	487	1121	151	0.400
Other costs	104	619	0	119	768	151	0.072
Total costs	2226	4946	868	2393	5714	1015	0.005

Note: Pre-Index period was for 6 months. Costs were calculated as an average per person and are adjusted to 2010 dollars using Consumer Price Index (CPI), rounded to nearest dollar.

(13,579), 21.2% did not receive any of the evaluated treatments for HMB; 78.8% of women underwent at least 1 treatment episode with 64.3% receiving only 1 treatment and 14.1% receiving only 2 treatments. For their initial treatment, the most commonly dispensed medication was OCs (12.1%) and high-dose oral progestins (9.5%), while the most common procedure was hysterectomy (27.8%) and endometrial ablation (23.6%). Of the 10,696 women with organic HMB who had at least 1 treatment, the most common second treatment was hysterectomy (10.3%) followed by UEA (4.3%); while 81.6% did not receive any further evaluated treatment.

For women with idiopathic HMB (*n* = 21,362), roughly one-third did not receive any of the evaluated treatments; 68.8% of women underwent at least 1 treatment episode with 57.6% receiving only 1 treatment and 10.9%

receiving only 2 treatments. For their initial treatment, the most commonly dispensed medication was OCs (18.3%) and high-dose oral progestins (9.9%), while the most common procedure was endometrial ablation (26.6%) and hysterectomy (10.3%). Of the 14,703 women with idiopathic HMB who received at least 1 treatment, the most common second treatment was hysterectomy (6.1%) followed by UEA (5.5%), while 3.7% did not receive any further evaluated treatment.

Overall All-Cause and HMB-Related Health Care Resource Utilization and Associated Costs

During the 6-month pre-index period, women in the organic cohort had significantly more physician ($P < 0.001$) and outpatient ($P = 0.001$) visits compared with the idiopathic cohort (Table 1). However, the median number of physician office visits was similar between the 2 cohorts (median 3.0) and there were few outpatient visits, inpatient admissions or ED visits (Table 1).

During the post-index period, the organic cohort had significantly more ($P < 0.001$) all-cause outpatient visits (7.3 vs. 6.2; median 5.0 and 5.0) and inpatient admissions (0.4 vs. 0.2), but similar all-cause physician office visits and ED visits compared to patients in the idiopathic cohort (**Table 2**). For post-index all-cause costs, women in the organic cohort had significantly higher total costs, contributed by the higher outpatient and inpatient medical costs, compared to women in the idiopathic cohort (Table 2).

Post-index HMB-related visits comprised only a small portion of the overall visits (**Table 3**). The organic cohort had significantly more HMB-related outpatient visits (2.0 vs. 1.7; median 2.0 and 1.0), and more inpatient admissions (0.3 vs. 0.1). For post-index HMB-related costs, women in the organic cohort had significantly higher total costs ($5727 vs. $3559), contributed by the higher inpatient medical costs, compared to the idiopathic cohort.

HMB-Related Health Care Resource Utilization and Associated Costs by Age

The follow-up HMB-related healthcare utilization and associated costs by age-groups for both the organic and idiopathic cohorts are shown in **Table 4**. For both cohorts, the total cost increased significantly with increasing age-group. In the organic cohort, the average HMB-related costs for women ages 18–34, 35–39, and 40–49 were $4891, $5577, and $5857, respectively. The increased costs were attributed to the increased number of inpatient visits and, to a lesser extent, physician office visits. In the idiopathic cohort, women ages 40–49 also had the highest average HMB-related costs among the 3 groups ($2644 for 18–34, $3755 for 35–39, and $3827 for 40–49). Similar to the organic cohort, the increased costs was partly attributed to the increase in inpatient visit. However, it was also due to higher outpatient visits and physician office visits.

One component of outpatient visit costs includes surgical procedures. When single episodes of HMB were evaluated (**Table 5**), the mean costs exceeded $8700 for a hysterectomy and $5000 for ablation. There were no significant differences identified among women with idiopathic HMB in different age-groups; however, age differences were identified in the organic HMB cohort in women having myomectomy procedures, with higher costs associated with women in the younger age-groups. Furthermore, women in the younger age-group (18–34 years) had significantly higher non–oral contraceptive costs compared with older women, while women aged 35–39 have significantly higher costs associated with high dose oral progestins.

Predicted Post-Index HMB-Related Costs

According to the results of a GLM analysis evaluating the relationship between cohort membership and post-index HMB-related costs (**Table 6**), the average costs for patients in the organic HMB cohort were expected to be 1.5 times higher than for the idiopathic cohort ($P < 0.001$). The predicted HMB-related costs were $5789 for the organic cohort and $3859 for the idiopathic cohort. For each additional year of age, patient costs were expected to increase. Higher Charlson comorbidity scores and additional treatment episodes were also expected to contribute to increased costs.

DISCUSSION

To our knowledge, this is the first study that examines the costs associated with treating HMB in a real-world setting using claims data. Overall, we find this population to be healthy, as indicated by the low Charlson comorbidity scores. The majority of women (63%) in this study sample of 34,941 patients were 40 to 49 years old. Generally, the women in this study did not have high rates of HMB-related visits to physicians, outpatient facilities, the hospital, or the ED, which may be the result of physicians not coding all the visits as HMB-related. Pharmacy costs were very low for both cohorts. In contrast, the costs for surgical procedures were high. The mean costs exceeded $8700 for a hysterectomy and $5000 for ablations. During the

Table 2. Post-Index All-Cause Health Care Utilization and Associated Costs by Cohort

Post-Index All-Cause Health Care Utilization and Costs by Cohort	Idiopathic (*n* = 21,362)			Organic (*n* = 13,579)			*P* Value
	Mean	SD	Median	Mean	SD	Median	
Health care utilization							
Physician office visits	15.7	14.1	12.0	15.9	15.0	12.0	0.340
Outpatient visits	6.2	6.6	5.0	7.3	6.8	5.0	< 0.001
ED visits	1.2	4.1	0.0	1.2	4.7	0.0	0.916
Inpatient admissions	0.2	0.5	0.0	0.4	0.6	0.0	< 0.001
Medical costs							
Physician office visits	2360	3196	1576	2396	3051	1594	0.291
Outpatient visits	4606	7823	2727	5612	9174	3788	< 0.001
ED visits	200	604	0	198	700	0	0.803
Inpatient admissions	2233	8028	0	4320	10,741	0	< 0.001
Pharmacy costs	1661	3313	643	1683	3452	623	0.572
Other costs	465	1887	165	586	2164	188	< 0.001
Total costs	11,526	14,734	7974	14,794	17,891	11,069	< 0.001

Note: Post-Index period was for 18 months. Costs were calculated as an average per person and are adjusted to 2010 dollars using Consumer Price Index (CPI), rounded to nearest dollar. ED = emergency department.

Table 3. Post-Index HMB-Related Health Care Utilization and Associated Costs by Cohort

Post-Index All-Cause Health Care Utilization and Costs by Cohort	Idiopathic (*n* = 21,362)			Organic (*n* = 13,579)			*P* Value
	Mean	SD	Median	Mean	SD	Median	
Health care utilization							
Physician office visits	2.2	1.5	2.0	2.2	1.5	2.0	0.021
Outpatient visits	1.7	1.9	1.0	2.0	2.0	2.0	< 0.001
ED visits	0.0	0.2	0.0	0.0	0.4	0.0	0.132
Inpatient admissions	0.1	0.3	0.0	0.3	0.5	0.0	< 0.001
Medical costs							
Physician office visits	454	717	269	425	613	275	< 0.001
Outpatient visits	1966	3281	214	2410	3593	882	< 0.001
ED visits	5	70	0	6	81	0	0.479
Inpatient admissions	981	3453	0	2718	5361	0	< 0.001
Pharmacy costs	70	182	0	44	144	0	< 0.001
Other costs	83	400	0	124	680	0	< 0.001
Total costs	3559	4574	1491	5727	5823	4230	< 0.001

Note: Post-Index period was for 18 months. Costs are calculated as an average per person and are adjusted to 2010 dollars using Consumer Price Index (CPI), rounded to nearest dollar. ED = emergency department.

Table 4. Follow-up HMB-Related Health Care Utilization and Costs by Cohort and Stratified by Age-Group

	Age-Group									
	18–34 years			35–39 years			40–49 years			
	Mean	SD	Median	Mean	SD	Median	Mean	SD	Median	*P* Value
Idiopathic cohort		(*n* = 4537)			(*n* = 4878)			(*n* = 11,947)		
Utilization										
Physician office visits	2.1	1.3	2.0	2.2	1.5	2.0	2.3	1.5	2.0	< 0.001
Outpatient visits	1.2	1.7	0.0	1.7	2.0	1.0	1.8	2.0	1.0	< 0.001
ED visits	0.0	0.2	0.0	0.0	0.2	0.0	0.0	0.2	0.0	< 0.001
Inpatient admissions	0.1	0.3	0.0	0.1	0.3	0.1	0.1	0.3	0.0	< 0.001
All-cause medical costs	2517	4325	622	3691	4463	1863	3776	4708	1940	< 0.001
Physician office visits	365	568	228	458	747	256	487	751	292	< 0.001
Outpatient visits	1389	2993	0	2198	3404	405	2091	3309	365	< 0.001
ED visits	9	101	0	4	42	0	5	65	0	< 0.001
Inpatient admissions	677	3001	0	940	3207	0	1112	3694	0	< 0.001
Pharmacy costs	128	233	0	64	172	0	50	157	0	< 0.001
Other costs	76	403	0	91	448	0	82	376	0	0.175
Total costs	2644	4287	898	3755	4441	1939	3827	4689	2003	< 0.001
Organic cohort		(*n* = 1114)			(*n* = 2435)			(*n* = 10,030)		
Utilization										
Physician office visits	2.1	1.5	2.0	2.1	1.5	2.0	2.2	1.5	2.0	0.004
Outpatient visits	1.9	1.9	2.0	2.0	1.9	2.0	2.0	2.0	2.0	0.159
ED visits	0.0	0.2	0.0	0.0	0.7	0.0	0.0	0.2	0.0	0.181
Inpatient admissions	0.2	0.4	0.0	0.3	0.5	0.0	0.3	0.5	0.0	< 0.001
All-cause medical costs	4807	5423	3127	5526	5666	4310	5819	5918	4306	< 0.001
Physician office visits	397	544	249	402	579	256	434	628	283	0.018
Outpatient visits	2179	3092	795	2568	3527	1110	2398	3659	854	0.009
ED visits	11	180	0	6	70	0	6	64	0	0.106
Inpatient admissions	2118	4912	0	2449	5140	0	2850	5454	0	< 0.001
Pharmacy costs	84	188	0	50	150	0	38	136	0	< 0.001
Other costs	101	397	0	102	503	0	132	740	0	0.083
Total costs	4891	5398	3227	5577	5643	4353	5857	5903	4328	< 0.001

Note: Costs are for the 18-month follow-up period and are adjusted to 2010 dollars using Consumer Price Index (CPI).

Table 5. Total HMB-Related Costs of Single-Episode Treatment Paths by Cohort and Stratified by Age-Group

	Age-Group									
	18–34 years (*n* = 4537)			35–39 years (*n* = 4878)			40–49 years (*n* = 11,947)			
	Mean	SD	Median	Mean	SD	Median	Mean	SD	Median	*P* Value
Idiopathic cohort										
Ablation	5290	3623	4423	5288	3514	4479	5133	3733	4385	0.342
Hysterectomy	8713	6338	8208	8980	5407	8339	9220	6042	8711	0.347
Myomectomy	3277	3909	1697	5065	3612	4228	3797	5095	2237	0.546
Oral contraceptives	1371	3122	822	1461	2145	927	1365	1682	936	0.694
High-dose oral progestins	1149	1674	499	1468	2145	597	1256	2194	599	0.278
Non-oral contraceptives	1036	1223	688	1431	3584	721	1151	1097	832	0.134
Organic Cohort										
Ablation	5395	4008	4582	5450	3411	4980	5145	3578	4386	0.182
Hysterectomy	9804	6350	8890	9109	6044	8572	9431	6339	8623	0.331
Myomectomy	4667	4146	3875	5550	4396	4722	4189	3780	3293	0.012
Oral contraceptives	2454	2981	1356	1974	2001	1081	2166	3091	1263	0.255
High-dose oral progestins	2933	2901	2075	3095	7782	921	1735	2157	819	0.002
Non-oral contraceptives	2538	2901	1291	1617	1255	1019	1585	1652	1050	0.021

Note: Costs are for the 18-month follow-up period and are adjusted to 2010 dollars using Consumer Price Index (CPI).

18 months post-index, the mean total medical costs were $2000 higher for patients in the organic cohort compared to the idiopathic cohort.

Furthermore, costs associated with multiple treatment paths were highest when hysterectomy was one of the treatments received (data not shown). This finding supports the results by You and colleagues [20], which demonstrated that hysterectomy was more costly than endometrial resection, ablation, and medical therapy 85% of the time. The elevated costs observed among women undergoing hysterectomy in the present study are also consistent with findings reported by Showstack and colleagues [21], who demonstrated that hysterectomy increased resource use significantly. In their study published in 2006, the mean cost for hysterectomy was $6777 compared with $4479 for medical treatment; furthermore, they estimated a mean total resource use of $6128 when hysterectomy was performed after the administration of medical treatment versus $2595 for women who remained on medical treatment.

A number of economic evaluations have been performed to compare the costs of medical versus surgical treatments [20–22] and to assess comparative costs of different medical treatments or different surgical treatments against each other [23–26], but the present study represents the most thorough evaluation of resource utilization and costs to date and is the first to compare the costs associated with specific types of healthcare utilization and specific medical and surgical treatments between patients with idiopathic and organic HMB. Furthermore, many of the previously published cost analyses are outdated [22,23,25–27] or pertain to expenditures in countries [20,27,28] other than the United States.

Study Limitations

Study limitations include those typical for retrospective claims data analysis, the limited length of the pre-index period (only

Table 6. GLM Analysis: Post-Index HMB-Related Costs

	Cost Ratio	95% Confidence Interval	*P* Value
Cohort			
Idiopathic cohort (ref group)			
Organic cohort	1.5	1.5, 1.5	< 0.001
Age	1.0	1.0, 1.0	< 0.001
Charlson Comorbidity Score	1.1	1.0, 1.1	< 0.001
Region			
Northeast (ref group)			
Midwest	1.2	1.2, 1.3	< 0.001
South	1.2	1.1, 1.3	< 0.001
West	1.1	1.0, 1.2	< 0.001
Episode counts	2.6	2.5, 2.6	< 0.001
Post-index diagnosis of pregnancy	0.8	0.8, 0.9	< 0.001

Note: Total n = 34,941 and 54 (0.15%) patients did not have post-index HMB-related costs. Generalized linear model (GLM) with gamma distribution and log-linked model.

Cohort	Predicted Post-Index HMB-related Costs (Mean)
Idiopathic cohort	$3859
Organic cohort	$5789

Note: Costs are for the 18-month follow-up period and are adjusted to 2010 dollars using Consumer Price Index (CPI).

6 months) to capture the true initial diagnosis of HMB, and lack of knowledge regarding reason for the choice of treatment. Patient choice of treatment may be based on future fertility options or treatment side effects [29], including impact on quality of life. Treatment patterns observed among these study patients may not fully reflect current treatment patterns in clinical practice with regard to medications taken such as tranexamic acid and LNG-IUS (which had not been approved for treatment of HMB during the study period). The costs may have underestimated the actual impact of heavy menstrual bleeding. Costs associated with over-the-counter medications (eg, NSAIDs) and hygiene items (eg, tampons, sanitary pads, diapers) are not captured in a claims database. Other complications/diagnosis may increase cost; a study by Morrison and colleagues found that more than 25% of women with HMB also had anemia and that higher treatment costs were incurred compared to women without anemia [30]. In addition, indirect costs related to days away from work or impact on daily activities were not captured. Only those procedures identified as being of interest were studied, and thus it is possible that not all procedures women with HMB typically undergo were captured; this may have led to under-representation of health care resource utilization and associated costs. On the other hand, an over-representation of health care utilization and costs may have resulted from the fact that the study population encompassed a high percentage of women with genital organ disorders (43.21%, data not shown), ie, women with HMB without such disorders may not have been as likely to seek treatment.

Conclusions

Although undiagnosed and untreated in many cases, HMB is a significant problem experienced by at least one-third of women at some point in their lives [8]. In addition to having an adverse impact on women's quality of life, productivity, and well-being, HMB can lead to increased health care resource utilization and associated costs. There is an unmet need for medical treatments with greater efficacy that can help more women avoid the potential risks and high costs of surgical procedures. Furthermore, women who wish to retain fertility may be better served by an effective medical regimen than by the typically more invasive surgical procedures that could pose a threat to future conception. Optimal treatment for

HMB requires a strategy that seeks to improve quality of life at a reasonable cost without compromising women's reproductive and overall health.

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