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ORIGINAL STUDY

Treatment and resource utilization for menopausal symptoms in the United States: a retrospective review of real-world evidence from US electronic health records

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Abstract

Objective: The aim of this study was to generate real-world evidence documenting use of prescription and nonprescription therapies recorded by health care providers for women experiencing vasomotor symptoms (VMS) associated with menopause.

Methods: This noninterventional, retrospective, observational cohort study used data from US patient medical records. Participating health care providers were gynecologists, internal medicine/family physicians, or advanced practice providers who typically saw three or more women per week presenting with menopausal symptoms and could identify eligible medical records; providers were recruited from local medical association directories and from listings from previously conducted research. Eligible women presented January 2016 through December 2019, were 40 to 60 years of age, and reported experiencing bothersome hot flashes at least twice within 24 hours.

Results: A total of 283 health care providers provided data for 1,016 women. The most common symptoms at initial presentation were hot flashes (91.2%), sleep problems (49.9%), and vaginal dryness (47.0%). At least one therapy for menopausal symptoms was recorded for 883 women (86.9%), and 611 (60.1%) had documentation of prescription medication, most commonly hormone therapy (70.4%). Nearly 40% of women had no prescription medication documented, and approximately 13% had no therapy documented. Despite experiencing bothersome menopausal symptoms, approximately 50% delayed seeking care for more than 6 months. Women had a mean of 2.1 (SD, 2.0) office visits related to menopause from initial presentation to completion of review, and health care resource utilization did not vary by treatment status. Subgroup analyses indicated nominal differences in treatment use across ethnic groups and varying prescribing patterns for menopausal symptoms by practitioner type and US region.

Conclusions: A high proportion of women with VMS remain untreated even when experiencing bothersome symptoms of menopause. Improved management of VMS is required to provide relief from the symptoms effectively and safely.

Key Words: Health care resource utilization – Hot flashes – Menopause – Night sweats – Retrospective medical record review – Vasomotor symptoms.

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Vasomotor symptoms (VMS), characterized by hot flashes (also called hot flushes) and night sweats, are among the most prevalent and troublesome symptoms of menopause.[1-3] An estimated 60% to 80% of US women experience VMS at some point during the menopausal transition, with the percentage varying with race and ethnicity.[1,4] According to the Study of Women's Health Across the Nation, an observational US study that included 3,302 multiracial/multiethnic women 42 to 52 years of age, VMS persist for a median of 7.4 years.[5] Other reports show that VMS are the most common menopausal symptoms for which women seek medical care,[6] and these symptoms substantially reduce health-related quality of life, particularly among women presenting with severe symptoms.[7] Women with VMS who do not seek care or are untreated have increased health care resource utilization (HCRU) and higher direct and indirect costs than women without VMS.[8]

Among current treatment options, estrogen-based hormone therapy (HT) is the most effective treatment for VMS.[9] Over the years, studies of HT, including the Women's Health Initiative, have suggested that HT is associated with an increased risk of stroke, breast cancer, and coronary heart disease.[10] Although these data have been inconsistent, many women in the menopausal transition need to or wish to avoid HT.[11] However, effective and well-tolerated treatment options for VMS remain limited, and current trends in the use of prescription and/or nonprescription (or complementary) therapies in the management of VMS are not well understood. The extent to which health care providers (HCPs) recommend and document the use of nonprescription therapies for VMS is also not clear, and the published literature reporting HCRU associated with VMS is lacking.

The current noninterventional, retrospective, observational cohort study aimed to identify and characterize the use of prescription and nonprescription therapies for VMS recorded by HCPs, bridge gaps in our knowledge of the treatment of VMS, and describe the broad spectrum of prescription and nonprescription therapies (including complementary therapies and behavioral/lifestyle modifications) used by women who experience VMS related to menopause. As a precursor to this analysis, qualitative interviews were performed in a small cross-section of representative HCPs (10 gynecologists, 10 primary care physicians [PCPs]). The interviews were designed to evaluate HCPs' perceptions of VMS treatment and related patient interactions. The results informed the development of the electronic data collection forms (DCF) that were used in the current study. Findings from that noninterventional, cross-sectional, observational study will be published separately in the next issue of *Menopause*.[12]

METHODS

Participants

The study was conducted by RTI Health Solutions (RTI-HS; Research Triangle Park, NC), in collaboration with the study sponsor (Astellas Pharma, Inc, Northbrook, IL). Participating HCPs were recruited from local medical association directories or from listings of previously conducted research (if they consented to be contacted for future studies) and were able to identify eligible medical records. Health care providers were gynecologists, internal medicine or family physicians, or advanced practice providers who typically consulted or treated at least three women per week presenting with menopausal complaints (including hot flashes), had prescriptive authority and access to and permission to use electronic health records (EHR) via the electronic system used by their practice, and practiced in the United States. Approximately 450 to 500 HCPs were invited to participate. Recruitment was guided by soft quotas to ensure that approximately 20% of the HCPs came from each US region (ie, Northeast, Southwest, West, Southeast, and Midwest) and that approximately 50% were practicing in gynecology and 50% in primary care.

Electronic health records from women initially presenting with menopausal complaints between January 1, 2016, and December 31, 2019, who were 40 to 60 years of age at the time of initial presentation and were residing in the United States were included in the analysis. The women also must have been experiencing bothersome hot flashes (defined as daytime or nighttime sensation of heat with sweating) two or more times within a 24-hour period. Women who experienced hot flashes for reasons other than menopause were excluded.

Study design

This EHR review was conducted using a noninterventional, retrospective, observational cohort study design. A quasi-random selection approach was used to select eligible EHR to the extent allowed by the facility's EHR system. The HCPs were requested to first identify women who met the study eligibility criteria and select one woman whose last name began with a randomly generated letter of the alphabet. The HCP then repeated this random selection process using another randomly generated letter to select the next woman. At sites where the EHR system did not allow this approach, the HCPs selected EHR of women who met the eligibility criteria from consecutive cases since January 1, 2016. The data from the patient EHR were captured by the HCP using a customized electronic DCF hosted on a secure Web-based data platform. Data captured in the DCF were guided by interviews with 20 HCPs who participated in initial qualitative interviews (interview results published separately in the next issue[12]). No identifying features were collected, and all data were coded (deidentified) using a unique study identification number generated by the data collection system. The DCF enabled internal data validity checks, giving immediate error alerts when out-of-range values were entered and promoting data completeness by preventing advancement to subsequent questions when required fields were not completed. The study was determined by RTI-HS International's institutional review board to meet the criteria for exemption from institutional review board review.

Study endpoints

The primary endpoint was all prescription and nonprescription therapies initiated for VMS as noted in the EHR, which contained a description of the therapy, therapy type (prescription, nonprescription, or both), each type of prescription therapy (inclusive of therapy combinations), route of administration (summarized separately for each prescription therapy type), prescription therapy change, prescription therapy patterns, nonprescription therapy initiated, nonprescription therapy change, prescription and

nonprescription therapy concomitantly initiated, and nonprescription therapy documentation.

Secondary endpoints were demographics, comorbidities, menopausal symptoms at the time of initial presentation with menopausal complaints, duration of menopausal symptoms, reasons for initial visit at which the patient presented with menopausal complaints, reasons for and type of treatment initiated for VMS, reasons for and type of treatment modifications, and health care resource use specific to menopause.

Subgroup analyses were also conducted to assess menopausal symptoms and current treatments documented for menopausal symptoms by ethnicity and to describe current treatment use by practitioner type (gynecologist vs PCP) and region of the United States.

Data analysis

Target recruitment was a minimum of 250 HCPs, who would each extract data from up to four patient records, to achieve a total of approximately 1,000 patient records. For demographics, prescription therapy, nonprescription therapy, and related treatment patterns, descriptive statistics included the number of patients (n), mean, SD, median, minimum, and maximum. Categorical data were summarized by frequencies and percentages and included reasons for therapy initiation, occurrence of outpatient visits, referrals to specialists (menopause specialists, gynecologists, and endocrinologists), and procedures such as hysteroscopy and endometrial biopsy for uterine bleeding, pelvic ultrasounds, blood tests, and visits to complementary or nontraditional HCPs. Menopause-specific HCRU was described for the overall population and as a function of treatment status.

RESULTS

HCP and patient demographic characteristics

A total of 283 HCPs participated in this cohort study. The majority were PCPs (42.8%) or gynecologists (37.8%) (Table 1). Health care providers had a mean age of 51 years, and a higher proportion were men (55.5%). Most HCPs practiced in the Southeast (24.7%), followed by the Northeast (24.0%), and the predominant primary practice setting was an office-based private clinic (86.6%). The HCPs had been in practice for a mean of 19.8 years since the end of their residency, and the mean number of adult women seen by these HCPs for menopause related complaints in a typical week was 32.8. Most HCPs (203 [72%]) abstracted data from at least four patients' EHR.

Health care providers provided data for a total of 1,016 women, among whom 611 (60.1%) had received a prescription medication for VMS, and 634 (62.4%) had documented use of nonprescription treatment for VMS in their EHR. The women had a mean age of 52.9 years, and the majority were White (71.0%), had completed at least some college (69.1%), and were privately insured (83%) (Table 1). Demographics were similar in the overall population and across subgroups by treatment status (ie, prescription only, nonprescription only, concomitant prescription and nonprescription, untreated).

Symptoms of menopause and comorbidities

Nearly 64% of women had at least one comorbidity. The most documented comorbidities (more than 5%) were hypertension (40.1%), headaches or migraines (18.1%), and uncomplicated diabetes (14.2).

Menopausal symptoms were the primary reason recorded for half (509 [50.1%]) of women for their initial presentation to an HCP (Fig. 1). Most of the remaining women first discussed their menopausal symptoms at regularly scheduled appointments. The menopausal symptoms recorded for at least 20% of the women at initial presentation were hot flashes (91.2%), followed by sleep problems (49.9%), vaginal dryness (47.0%), mood changes (44.6%), reduced libido (32.5%), dyspareunia (26.9%), and weight gain/slowed metabolism (25.5%) (Fig. 2). The mean number of symptoms reported at the initial presentation was 4.2. Nearly half of the women (513 [50.5%]) had been experiencing symptoms for at least 6 months before initial presentation, 326 (32.1%) for 3 to 6 months, and 161 (15.8%) for up to 3 months.

Prescription and nonprescription therapies for menopausal symptoms

Of the 1,016 women in the overall population, 249 (24.5%) had documentation of only prescription therapy, 272 (26.8%) of only nonprescription therapy or intervention, and 362 (35.6%) of both prescription and nonprescription therapy or intervention. Eight hundred eighty-three women (86.9%) had documentation of at least one therapy or intervention for symptoms associated with menopause in their EHR.

Of the 611 women (60.1%) who received prescription therapy for menopausal symptoms (either alone or in combination with nonprescription therapy), hormone therapy was the most commonly prescribed (430 [70.4%] or 42.3% of the total population) (Fig. 3A). This included systemic estrogen (188 [30.8%]), combination estrogen/progestogen (202 [33.1%]), local estrogen (42 [6.9%]), and progesterone (30 [4.9%]). Compounded HT was prescribed to 76 women (12.4%) and included estrogen/progestogen (26 [4.3%]), estrogen/progestogen/testosterone (16 [2.6%]), testosterone (16 [2.6%]), systemic estrogen (10 [1.6%]), estrogen/testosterone (8 [1.3%]), progesterone (5 [0.8%]), and local estrogen (5 [0.8%]).

Selective serotonin reuptake inhibitors (SSRIs) and serotonin and norepinephrine reuptake inhibitors (SNRIs) were prescribed to 89 (14.6%) and 40 (6.5%) women, respectively. Selective serotonin reuptake inhibitors included paroxetine (32 [5.2%]), fluoxetine (20 [3.3%]), sertraline (19 [3.1%]), escitalopram (14 [2.3%]), and citalopram (7 [1.1%]), and SNRIs included venlafaxine (29 [4.7%]), duloxetine (8 [1.3%]), and desvenlafaxine (3 [0.5%]). Other less frequently prescribed treatments included clonidine (27 [4.4%]), gabapentin/pregabalin (25 [4.1%]), and selective estrogen-receptor modulators (4 [0.7%]). Selective estrogen-receptor modulators included raloxifene (2 [0.3%]) and bazedoxifene/conjugated estrogens (2 [0.3%]). In addition, there was one prescription (0.2%) each recorded for bupropion, oxybutynin, zolpidem, methylprednisolone, propranolol, and oral contraceptive pills.

Among the 634 women (62.4%) with documentation of nonprescription therapies or interventions, herbal, vitamin, traditional

TABLE 1. *HCP and patient demographic characteristics*

HCP demographic characteristics	n = 283
Age, y	
Mean (SD)	51.1 (9.1)
Sex, n (%)	
Male	157 (55.5)
Female	119 (42.0)
Nonbinary/third gender	2 (0.7)
Prefer not to answer	5 (1.8)
Medical specialty, n (%)	
Gynecologists	107 (37.8)
PCPs	121 (42.8)
Advanced practice providers, gynecologists	24 (8.5)
Advanced practice providers, PCPs	31 (11.0)
Primary practice setting, n (%)	
Office-based private clinic	245 (86.6)
Hospital based: academic or teaching	15 (5.3)
Hospital based: community	15 (5.3)
Other[a]	8 (2.8)
Region, n (%)	
Midwest	53 (18.7)
Northeast	68 (24.0)
Southeast	70 (24.7)
Southwest	34 (12.0)
West	58 (20.5)
Years in practice (postresidency or post–board certification)	
Mean (SD)	19.8 (7.6)
Adult women seen for menopausal complaints in typical week	
Mean (SD)	32.8 (23.8)
Patient demographic characteristics	**n = 1,016**
Age, y	
Mean (SD)	52.9 (4.4)
Race, n (%)	
White	721 (71.0)
Black	167 (16.4)
Asian, Native American, or Alaska Native	83 (8.2)
Other (includes Hispanic/Mexican/Latina, Native Hawaiian or other Pacific Islander, and Turkish)	35 (3.4)
Prefer not to answer/not documented in EHR	10 (1.0)
Body mass index, kg/m^2 (n = 972)	
Mean (SD)	27.3 (4.7)
Smoking status, n (%)	
Never	659 (64.9)
Former	255 (25.1)
Current	87 (8.6)
Not documented in EHR	15 (1.5)
Highest education level, n (%)	
High school degree or less	187 (18.4)
Some college, associate's degree, or bachelor's degree	550 (54.1)
Master's or higher-level degree	152 (15.0)
Not documented in EHR	127 (12.5)
Documented therapy, n (%)	
Prescription only	249 (24.5)
Nonprescription only[b]	272 (26.8)
Prescription and nonprescription[b]	362 (35.6)
None documented	133 (13.1)
Insurance type, n (%)	
Private	843 (83.0)
Medicare	51 (5.0)
Medicaid	92 (9.1)
Tricare	2 (0.2)
Uninsured	20 (2.0)
Not documented	8 (0.8)

EHR, electronic health record; HCP, health care provider; PCP, primary care physician. [a]Other includes private hospital (n = 5) and federally qualified health center, skilled nursing facility, and hospital and office (n = 1 for each). [b]Nonprescription therapies included herbal, vitamin, traditional Chinese therapies, supplements, complementary and alternative therapy (eg, acupuncture, hypnosis, cognitive-behavioral therapy), behavioral/lifestyle interventions, and other strategies (eg, vaginal lubricant, postcoital hygiene measures, layered clothing, psychotherapy, increased hydration).

Chinese therapies, or supplements were recorded for 347 women (54.7%) (Fig. 3B). In this category, the most common therapy was black cohosh, recorded for 190 women (30.0%; 18.7% of the total population). Complementary and alternative therapies (eg, acupuncture, hypnosis, cognitive-behavioral therapy) were recorded for 67 women (10.6%), and behavioral/lifestyle interventions were recorded for 314 (49.5%), for whom exercise was the most commonly recorded (264 [41.6%]). Seventeen women (2.7%) had other strategies recorded; these included vaginal lubricant, postcoital hygiene measures, layered clothing, psychotherapy, and increased hydration. The specific type of nonprescription therapy was not documented for 40 women (6.3%).

Table 2 presents the reasons for initiating and modifying select prescription and nonprescription treatments for symptoms of menopause. Efficacy was the most common reason for initiating and modifying most prescription therapy. Women with a prescription for noncompounded estrogen/progestogen combination rarely required treatment modification (34/202 [16.8%]). After efficacy, the most commonly reported reasons for initiating black cohosh, were patient beliefs and/or perceptions (94/190 [49.5%]) and advice or experience from family or friends (51/190 [26.8%]); HCP recommendation was rarely recorded as the reason for initiating black cohosh (18/190 [9.5%]).

The most commonly reported routes of administration for any type of prescription HT were oral and transdermal (Fig. 4). Although the prescribed hormone was usually systemic, vaginal HT was also prescribed for menopausal symptoms.

Menopause-specific HCRU

Women had a mean of 2.1 (SD, 2.0) office visits related to menopause from initial presentation to completion of the review. Health care resource utilization did not seem to vary substantially by treatment status (Fig. 5). Overall, referrals to gynecologists were documented for 265 women (26.1%), referrals to menopause specialists for 51 women (5.0%), and referrals to endocrinologists for 34 women (3.3%). The most frequently documented procedure was pelvic ultrasound (204 [20.1%]). Hysteroscopy (51 [5.0%]), endometrial biopsy for uterine bleeding (81 [8.0%]), and hysterectomy (3 [0.3%]) were uncommon. A total of 466 women (45.9%) had a blood test related to menopausal complaints. Nontraditional or complementary health care visits were recorded for 111 women (10.9%). Other documented procedures included a NovaSure endometrial ablation and a Papanicolaou smear for one woman each.

Subgroup analyses

Menopausal symptoms and treatment by race

Data extracted from EHR of 1,006 women included information about race/ethnicity: 721 women were White; 167 were Black/African American; 83 were Asian, Native American, or Alaska Native; and 35 were of other ethnic origins (Native Hawaiian/Pacific Islander, Hispanic/Mexican/Latina, and Turkish). Demographics by race/ethnicity were similar between groups, with the exception of insurance type and presence of comorbidities. A greater percentage of White (88.1%) and Asian/Native American/Alaska Native women (84.3%) had private insurance

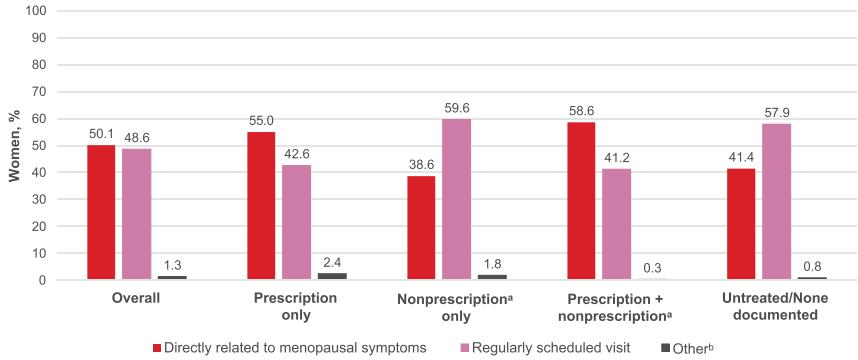

FIG. 1. Primary reason for initial presentation to an HCP as documented in medical records of women selected in this observational study overall and by documented treatment. [a]Nonprescription therapies include herbal, vitamin, traditional Chinese therapies, supplements, complementary and alternative therapy (eg, acupuncture, hypnosis, cognitive-behavioral therapy), behavioral/lifestyle interventions, and other strategies (eg, vaginal lubricant, postcoital hygiene measures, layered clothing, psychotherapy, increased hydration). [b]Other reasons for visit included to establish care, postoperative care, weight loss, and specific symptoms or conditions (chest pain, dyspnea, dysuria, hypertensive urgency, panic disorder, pelvic pain, and urinary tract infection). HCP, health care provider.

compared with Black women (67.7%), whereas a higher proportion of Black women (22.2%) had Medicaid (vs 5.5% of White and 6.0% Asian/Native American/Alaska Native women); 1.1% of White, 0.6% of Black, and 7.2% of Asian/Native American/Alaska Native women were uninsured. Black women were more likely to have comorbidities than White and Asian/Native American/Alaska Native women (83.8% vs 59.9% and 49.4%, respectively).

At the initial visit, the most commonly reported symptoms of menopause for women of all races were hot flashes, followed by sleep problems, vaginal dryness, mood changes, reduced libido, dyspareunia, and weight gain/slowed metabolism (Table 3). Nominal differences were noted for specific symptoms; for example, Black women reported more vaginal dryness than did women in the other groups (53.9% vs 40.0%-45.9%) and Asian/Native American/Alaska Native women reported more thinning/dry hair (21.7% vs 9.0%-14.8%). A higher proportion (62.9%) of Black women experienced symptoms for more than 6 months compared with approximately 50% of women in the other groups. Asian/Native American/Alaska Native women less commonly had prescription medications documented (49.4%) compared with women in all other groups (ie, White, 61.2%; Black, 62.9%; and other, 54.3%) and more commonly had nonprescription therapies documented (71.1%) compared with all other groups (White, 62.6%; Black, 58.1%; and other, 62.9%). In addition, White women more commonly received HT (ie, systemic estrogen, combination estrogen/progestogen, local estrogen, and progesterone), and Black women more commonly received compounded HT (ie, estrogen/progestogen, estrogen/progestogen/testosterone, testosterone, systemic estrogen, estrogen/testosterone, progesterone, and local estrogen).

Among women receiving prescription medication, 73.9% and 11.3% of White women, 60.0% and 18.1% of Black women, and 68.3% and 9.8% of Asian/Native American/Alaska Native women received HT and compounded HT, respectively (Table 3). Use of SSRIs was lowest among Asian/Native American/Alaska Native women (7.3%) compared with all other groups (14.5%-16.2%).

Treatment by practitioner type and region

Data were abstracted by 131 gynecologists and 152 PCPs. Gynecologists (includes gynecologists and advanced practice providers) abstracted data from the EHR of 512 women, and PCPs (includes PCPs and advanced practice providers) abstracted data from the EHR of 504 women. Characteristics of gynecologists and PCPs were similar, with a mean age of approximately 51 years and a mean number of years in practice of approximately 20; most HCPs were in office-based private practice (80.9% of

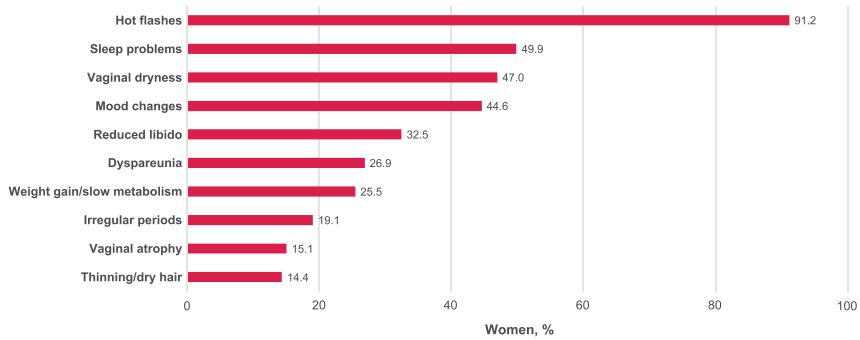

FIG. 2. Top 10 menopausal symptoms recorded for women selected in this observational study. Women with more than one symptom were counted in multiple categories.

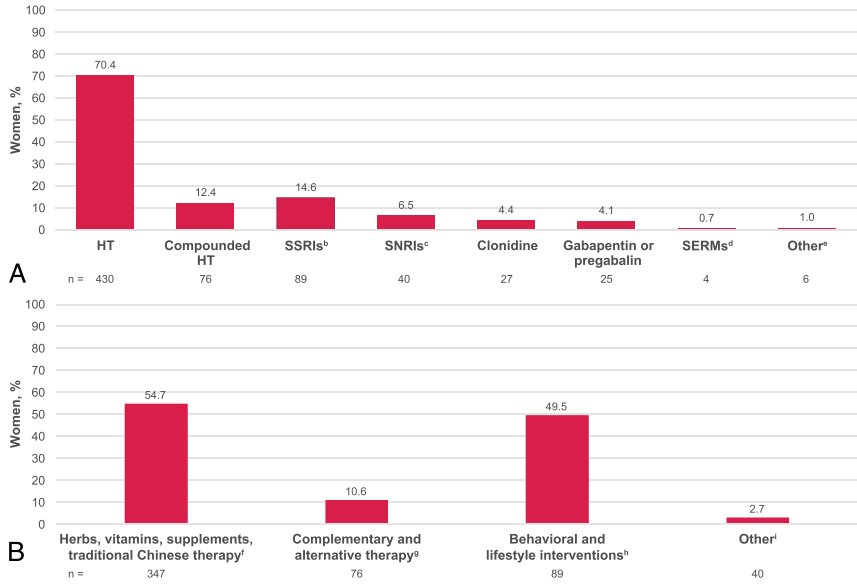

FIG. 3. Type and proportion of prescription therapy[a] (**A**) and nonprescription treatments (**B**) received by the women for symptoms of menopause. [a]Women with more than one documented prescription therapy were counted in multiple categories. Most (88%) women prescribed treatment for menopausal symptoms received one prescription at a time. [b]SSRIs included paroxetine (32 [5.2%]), fluoxetine (20 [3.3%]), sertraline (19 [3.1%]), escitalopram (14 [2.3%]), and citalopram (7 [1.1%]). [c]SNRIs included venlafaxine (29 [4.7%]), duloxetine (8 [1.3%]), and desvenlafaxine (3 [0.5%]). [d]SERMs included raloxifene (2 [0.3%]) and bazedoxifene/conjugated estrogens (2 [0.3%]). [e]Other prescription treatments included one (0.2%) each of bupropion, oxybutynin, zolpidem, methylprednisolone, propranolol, and oral contraceptive pills. [f]Ten most common: black cohosh (190 [30.0%]), Estroven plant-based supplement containing rhapontic rhubarb (81 [12.8%]), evening primrose oil (70 [11.0%]), vitamin E (62 [9.8%]), magnesium (42 [6.6%]), phytoestrogens (26 [4.1%]), valerian (23 [3.6%]), isoflavones (13 [2.1%]), red clover (10 [1.6%]), and maca (7 [1.1%]). [g]Complementary and alternative therapy included acupuncture (38 [6.0%]), cognitive-behavioral therapy (31 [4.9%]), hypnosis (2 [0.3%]), and functional medicine consult (1 [0.2%]). [h]Behavioral and lifestyle interventions included exercise (264 [41.6%]), food or alcohol avoidance (170 [26.8%]), sleep alterations (eg, cooling sheets, pillows, sleepwear) (165 [26.0%]), and type of behavioral/lifestyle intervention undocumented (62 [9.8%]). [i]Other includes vaginal lubricant (12 [1.9%]), layered clothing (2 [0.3%]), postcoital hygiene (1 [0.2%]), psychotherapy (1 [0.2%]), and increased hydration (1 [0.2%]). HT, hormone therapy; SERM, selective estrogen receptor modulator; SNRI, serotonin norepinephrine reuptake inhibitor; SSRI, selective serotonin reuptake inhibitor.

gynecologists and 91.4% PCPs). However, more PCPs were male (60.5% vs 49.6% gynecologists), and gynecologists saw more patients per week for menopausal complaints.

Examination of patient records showed that reported menopausal symptoms did not generally differ by HCP type, although patients of gynecologists had more vaginal and sexual

TABLE 2. *Reasons for initiating and modifying select prescription and nonprescription treatments for symptoms associated with menopause*

	Noncompounded estrogen/progestogen (n = 202)	Systemic estrogen (n = 188)	Paroxetine (n = 32)	Venlafaxine (n = 29)	Black cohosh (n = 190)
Top reasons for treatment initiation, n (%)					
Considered to have good efficacy	100 (49.5)	84 (44.7)	14 (43.8)	15 (51.7)	41 (21.6)
Patient beliefs/perceptions	50 (24.8)	49 (26.1)	7 (21.9)	5 (17.2)	94 (49.5)
HCP recommendation	85 (42.1)	78 (41.5)	11 (34.4)	10 (34.5)	18 (9.5)
Consideration of potential adverse effects	31 (15.3)	17 (9.0)	5 (15.6)	6 (20.7)	12 (6.3)
Advice/experience of family and/or friends	24 (11.9)	27 (14.4)	2 (6.3)	5 (17.2)	51 (26.8)
Treatment modification made, n/N (%)	34/202 (16.8)	36/188 (19.1)	7/32 (21.9)	11/29 (37.9)	52/190 (27.4)
Dose adjusted	21/34 (61.8)	27/36 (75.0)	4/7 (57.1)	10/11 (90.9)	7/52 (13.5)[a]
Dose increased	17/34 (50.0)	22/36 (61.1)	4/7 (57.1)	10/11 (90.9)	—
Dose reduced	4/34 (11.8)	5/36 (13.9)	0	0	—
Treatment switch	3/34 (8.8)	4/36 (11.1)	2/7 (28.6)	0	0
Treatment added	1/34 (2.9)	3/36 (8.3)	0	0	0
Other/switch to PO	2/34 (5.9)	0	0	0	0
Medication discontinued	8/34 (23.5)	2/36 (5.6)	1/7 (14.3)	1/11 (9.1)	45/52 (86.5)
Reason for treatment modification, n/N (%)					
Lack of efficacy	15/34 (44.1)	22/36 (61.1)	7/7 (100.0)	8/11 (72.7)	38/52 (73.1)
Patient decision	13/34 (38.2)	8/36 (22.2)	0	1/11 (9.1)	14/52 (26.9)
Tolerability/AEs	4/34 (11.8)	1/36 (2.8)	2/7 (28.6)	0	0
Consideration for potential AEs	3/34 (8.8)	2/36 (5.6)	0	1 (9.1)	0
Duration of therapy	1/34 (2.9)	2/36 (5.6)	0	1 (9.1)	0
Financial concerns	2/34 (5.9)	1/36 (2.8)	0	0	4/52 (7.7)
HCP recommendation	7/34 (20.6)	2/36 (5.6)	0	4/11 (36.4)	5/52 (9.6)

AE, adverse event; HCP, health care provider.
[a]Captured only as a "dose adjustment."

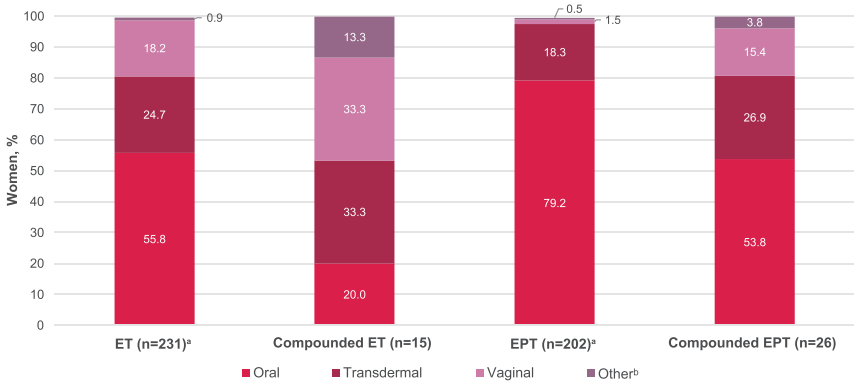

FIG. 4. Route of administration for most common prescription hormone therapies. [a]Route of administration was not documented in the medical record of one woman who received ET and one who received EPT. [b]Other includes SC, percutaneous, and IM. EPT, estrogen/progestogen therapy; ET, estrogen therapy; IM, intramuscular; SC, subcutaneous.

symptoms recorded than patients of PCPs. Gynecologists' patients more commonly had prescription medications documented (63.5% vs 56.7%) and less commonly had nonprescription therapy or intervention documented (58.8% vs 66.1%) compared with PCPs' patients.

Of women with documented prescription therapies, gynecologists' patients more often received HT (76.3% vs 63.6%) and compounded HT (17.2% vs 7.0%) and less often received SSRIs (10.8% vs 18.9%) and SNRIs (1.8% vs 11.9%) than PCPs' patients. Among women with documented nonprescription therapies or interventions, black cohosh was more frequently documented by PCPs (35.1%) than gynecologists (24.3%), whereas Estroven was more frequently documented by gynecologists (15.6%) than PCPs (10.2%). Hormone therapy was prescribed by 75.0% of physicians in the Midwest, 69.4% in the Northeast, 64.8% in the Southeast, 70.7% in the Southwest, and 73.1% in the West. Compounded HT prescriptions were more common in the Southeast (20.0%) and Southwest (19.6%) than in the West (11.2%), Midwest (7.8%), and Northeast (4.0%), and SSRI use was more common in the Northeast (21.8%) than in the Midwest (12.1%), Southeast (15.2%), Southwest (13.0%), and West (10.4%). There were nominal differences in insurance coverage by region. The Southeast and Southwest had the highest proportion of patients with private insurance (88.5% and 86.2%, respectively) compared with the West, Northeast, and Midwest (79.2%, 80.9%, and 81.1%, respectively). Women in the Southeast and Southwest were more likely to have had prior hysterectomy than women in other regions (25.6% and 26.9% vs 13.9% to 15.4%, respectively).

DISCUSSION

The findings of this noninterventional, retrospective, observational cohort study based on data abstracted from 1,016 patient EHR conducted to assess the management of VMS among women in menopause showed that HT for menopausal complaints was prescribed to 42.3% (430 of the 1,016 women overall); however, 39.9% (405/1,016) had no prescription medication documented, and 13.1% (133/1,016) had no treatment of any kind documented. Despite experiencing an average of four menopausal symptoms, half of the women delayed seeking care for at least 6 months. Utilization of health care resources did not differ by prescription or nonprescription treatment status. Our findings are consistent with those from previous studies reporting that many women in menopause wish to avoid hormonal treatment or do not consider it an option for alleviating VMS.[11]

In addition, women experiencing bothersome hot flashes also commonly report myriad other symptoms, especially sleep problems, emotional/mood changes, and vaginal problems. In a recent cross-sectional qualitative study, sleep disturbance was reported by 93.8% of women in the United States who were experiencing

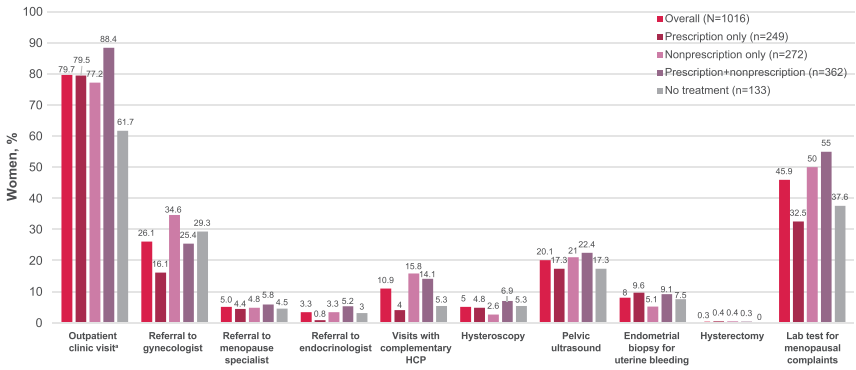

FIG. 5. Menopause-specific health care resource utilization by documented treatment status. [a]Some outpatient visits may not have been captured by the provider. HCP, health care provider.

TABLE 3. *Symptoms associated with menopause and therapies by race*

Characteristic	White (n = 721)	Black or African American (n = 167)	Asian/Native American/Alaska Native (n = 83)	Other race/ethnicity[a] (n = 35)
Menopausal symptoms (occurring in >10% of women), n (%)				
Hot flashes	667 (92.5)	150 (89.8)	73 (88.0)	31 (88.6)
Vaginal dryness	331 (45.9)	90 (53.9)	38 (45.8)	14 (40.0)
Vaginal atrophy	102 (14.1)	32 (19.2)	13 (15.7)	2 (5.7)
Dyspareunia	193 (26.8)	49 (29.3)	21 (25.3)	8 (22.9)
Mood changes	325 (45.1)	69 (41.3)	39 (47.0)	16 (45.7)
Sleep problems	369 (51.2)	76 (45.5)	37 (44.6)	21 (60.0)
Urinary problems	65 (9.0)	21 (12.6)	11 (13.3)	8 (22.9)
Irregular periods	128 (17.8)	26 (15.6)	25 (30.1)	14 (40.0)
Weight gain or slowed metabolism	184 (25.5)	50 (29.9)	16 (19.3)	9 (25.7)
Thinning/dry hair	107 (14.8)	15 (9.0)	18 (21.7)	5 (14.3)
Dry skin	91 (12.6)	20 (12.0)	11 (13.3)	5 (14.3)
Reduced libido	250 (34.7)	45 (26.9)	20 (24.1)	12 (34.3)
Difficulty concentrating	103 (14.3)	24 (14.4)	7 (8.4)	5 (14.3)
Duration of symptoms, n (%)				
≤3 mo	117 (16.2)	13 (7.8)	20 (24.1)	6 (17.1)
3-6 mo	247 (34.3)	48 (28.7)	21 (25.3)	10 (28.6)
6-12 mo	222 (30.8)	69 (41.3)	22 (26.5)	12 (34.3)
>12 mo	121 (16.8)	36 (21.6)	19 (22.9)	7 (20.0)
Not documented	14 (1.9)	1 (0.6)	1 (1.2)	0
Documented therapy, n (%)				
Prescription only	183 (25.4)	42 (25.1)	13 (15.7)	8 (22.9)
Prescription and nonprescription	258 (35.8)	63 (37.7)	28 (33.7)	11 (31.4)
Nonprescription only	193 (26.8)	34 (20.4)	31 (37.3)	11 (31.4)
Prescription treatments, n (%)	441 (61.1)	105 (62.9)	41 (49.4)	19 (54.3)
Hormone therapy (any)	326 (73.9)	63 (60.0)	28 (68.3)	11 (57.9)
Compounded hormone therapy (any)	50 (11.3)	19 (18.1)	4 (9.8)	3 (15.8)
SSRIs	64 (14.5)	17 (16.2)	3 (7.3)	3 (15.8)
SNRIs	32 (7.3)	5 (4.8)	2 (4.9)	0
Clonidine	18 (4.1)	6 (5.7)	2 (4.9)	1 (5.3)
Gabapentin or pregabalin	17 (3.9)	5 (4.8)	4 (9.8)	0
SERMs	3 (0.7)	0	0	1 (5.3)
Other	5 (1.1)	1 (1.0)	0	0
Nonprescription treatments documented (in >15% of women in any group), n (%)	451 (62.6)	97 (58.0)	59 (71.1)	22 (62.9)
Black cohosh	153 (33.9)	17 (17.5)	12 (20.3)	6 (27.3)
Estroven	53 (11.8)	12 (12.4)	9 (15.3)	3 (13.6)
Vitamin E	45 (10.0)	6 (6.2)	10 (16.9)	1 (4.5)
Exercise	196 (43.5)	37 (38.1)	21 (35.6)	9 (40.9)
Sleep alterations	119 (26.4)	29 (29.9)	11 (18.6)	6 (27.3)
Food or alcohol avoidance	126 (27.9)	27 (27.8)	10 (16.9)	6 (27.3)

SERM, selective estrogen-receptor modulator; SNRI, serotonin norepinephrine reuptake inhibitor; SSRI, selective serotonin reuptake inhibitor.
[a]Native Hawaiian/Pacific Islander, Hispanic/Mexican/Latina, and Turkish.

moderate to severe VMS related to menopause; however, the participants did not report a problem falling asleep initially, but experienced frequent sleep interruptions due to physical discomfort from profuse sweating and overheating.[13]

Systemic HT is the treatment for VMS associated with menopause recommended by The North American Menopause Society and the American College of Obstetricians and Gynecologists.[14,15] In the current observational study, 60.1% (611/1,016) of women experiencing VMS received a prescription therapy, with systemic HT being the most common. Initiation of a prescription therapy did not seem to be related to symptom type, as we noted similar proportions of women reporting specific symptoms irrespective of whether they had prescription therapy. The exception was mood changes, such that a smaller proportion of women who did not initiate any type of therapy (including nonprescription) reported this symptom. Among women who received an SSRI/SNRI, 61.9% (78/126) reported mood changes, whereas 38.1% (48/126) did not. Thus, initiation of therapy may be driven by a patient risk-benefit assessment, with symptom severity and interference being key drivers. The North American Menopause Society and the American College of Obstetricians and Gynecologists also recommend the use of nonhormonal therapies, including SSRIs, SNRIs, gabapentin, pregabalin, and clonidine as alternatives to hormone therapy,[15,16] and paroxetine is specifically approved for VMS.[17,18] In this study, 14.6% (89/611) of women with a prescription received an SSRI, either paroxetine, fluoxetine, sertraline, escitalopram, or citalopram. Thus, although SSRIs are recommended to reduce the frequency and severity of hot flashes, our study showed that these medications were not commonly prescribed by HCPs in the management of VMS but were more commonly prescribed by PCPs than gynecologists.

We also found that 62.4% (634/1,016) of patients had a nonprescription therapy or intervention documented in their EHR, suggesting that HCPs discuss complementary and alternative approaches to symptom management with their patients. The

most documented therapy was black cohosh; however, the reason for initiating black cohosh was primarily patient preference and rarely HCP recommendation. Overall, the primary reason that providers prescribed a therapy was efficacy, and the primary reason they modified treatment was lack of efficacy. Gynecologists' patients more often had prescription medications and less often had nonprescription medications documented compared with PCPs' patients. This suggests that PCPs may be more comfortable with complementary therapies or may be more likely to document them. It is also possible that patients seeking the care of a gynecologist may have more bothersome symptoms associated with menopause, leading to more use of prescription therapy.

We also looked at symptoms and treatment by patient ethnicity. Whereas experience with menopausal symptoms was similar across ethnic groups, some differences were observed in treatment use. The majority of Black women experienced menopausal symptoms longer than women of other ethnicities before seeking treatment, and women who were Asian, Native American, or Alaska Natives were more likely to take nonprescription therapies and less likely to have documentation of prescription medications. White women were most likely to have received HT, which is the current standard of care, suggesting that there is room for improvement in treating women of color.

Limitations and strengths

The results of this study must be interpreted with caution as retrospective EHR review studies have a number of limitations. The women selected in this study may not represent the general population of women experiencing VMS, and the HCPs who participated in the study may have been more willing to diagnose and treat VMS. Demographic characteristics of our HCP and patient populations generally align with available US population statistics; however, our sample may have had a lower proportion of female HCPs (42% in the current study vs 46% of PCPs and 85.2% of gynecologists) and fewer women who were uninsured (2% in the current study vs 13% in women aged 18-64 years nationally).[19-26] In addition, the data were limited to information available in the EHR, and therefore, any information on nonprescription medications that were not reported to HCPs or not recorded by HCPs was unavailable for this study. Consequently, the proportion of women initiating nonprescription therapy may be underestimated. In addition, the inclusion criteria of two or more bothersome hot flashes in 24 hours led to the inclusion of women with milder symptoms. The number of patients receiving prescription or nonprescription treatment may be higher in women with more frequent or severe VMS. Symptom severity was noted as a key factor for HCP treatment selection in the qualitative interviews conducted as part of this study.[12] Data entered may also be subject to entry errors, resulting in inaccuracies in the EHR. Although data checks were conducted to assess internal consistency of the entered data, the responses were not validated by an independent reviewer. The inclusion of EHR from patients who were seeing gynecologists or PCPs and the geographic and ethnic diversity of the patients across the United States are strengths of this study.

CONCLUSIONS

Research associated with the management of VMS suggests that the use of prescription and nonprescription therapies for VMS associated with menopause is not well understood. The current study provides strong evidence on the current management of VMS, the extent to which nonprescription therapy is documented in the EHR, and the HCRU associated with VMS in the United States. These data can help HCPs improve the management of VMS related to menopause and help fill the knowledge gaps to improve the care of women in the menopausal transition.

The findings of the current study confirm that despite the availability of prescription and nonprescription treatment options, a substantially high proportion of women experiencing VMS remain untreated even when experiencing bothersome symptoms of menopause. Improved management is required to provide relief from VMS effectively and safely. In addition, women may benefit from education or encouragement to report symptoms as they emerge.

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