Cross-sectional Study of Women with Menopause-associated Vasomotor Symptoms in Mexico – WARM Study

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ABSTRACT

Introduction: A large majority of women may spend a significant part of their lives in the postmenopausal stage. Transition to menopause usually represents a milestone affecting their quality of life. Vasomotor symptoms are characterized by hot flashes and/or night sweats.

Objective: This study used a survey intended to determine the prevalence of moderate to severe vasomotor symptoms and to collect data to evaluate the associated economic burden through the collection of healthcare resource utilization, as well as the number of women seeking medical advice (primary care and different types of specialty healthcare professionals), number of women receiving drug therapy and calculating out-of-pocket expenses.

Methods: Cross-sectional study in peri- and postmenopausal women aged 40 to 65 years with moderate to severe menopause-associated vasomotor symptoms in Mexico, as a sub-study of the NCT05083884 clinical trial. An active panel was used to identify participants, who filled an online survey regarding the symptoms they experienced in the previous week, how it impacts their quality of life, sleep pattern, and their interactions with healthcare professionals.

Results: A total of 7,728 women were contacted, of whom 1,697 were selected; 412 filled out the survey, of which 17% presented vasomotor symptoms. Most of them experienced more than 3 symptoms, affecting their work and non-work-related activities by 5.9% and 35.7%, respectively. Furthermore, 78.4% of respondents sought medical care. Over 50% of women reported being on some type of treatment.

Conclusions: In accordance with other studies, an elevated proportion of women was found to experience moderate to severe vasomotor symptoms, and these symptoms had an impact on their quality of life.

KEYWORDS

Vasomotor symptoms, menopause, menopausal transition, women, Mexico.

Introduction

Life expectancy for women is increasing progressively worldwide. Mean life expectancy for women in the United States is 80 years, while women who are currently 75 years old can expect 12.4 additional years of life [1]. Life expectancy has also increased for Mexican women, to 80 ± 3.82 years [2,3].

Menopause is defined as the final menstrual period (FMP) and is usually confirmed when a woman has had amenorrhea for 12 consecutive months. The mean age at which this occurs in the United States is 51.3 years, ranging between 43.8 and 53.0 years [4-6]. Among women residing in Mexico, menopause occurs at 47.9 years on average [2]. Factors associated with an earlier onset of menopause include: low economic income, low level of education, living more than 2,000 meters above sea level, having a body mass index (BMI) higher than 30 kg/m^2, and the lack of physical activity [3-8].

Vasomotor symptoms, commonly described as hot flushes, is the most common symptom experienced by up to 80% of women transiting the menopause and after [9]. A large majority of women rate their vasomotor symptoms as moderate to severe and describe their experience as a sensation of heat with sweating [10,11]. Symptoms persist for a mean of 7 to 10 years, although this seems to depend on the time of onset [12,13].

The impact of vasomotor symptoms in women is related with sleep alterations, fatigue, anxiety, and depression, which can impair the development of daily and work activities [14-17].

The purpose of this study was to design and deploy a survey for peri- and postmenopausal women aged 40 to 65, to determine the prevalence of moderate to severe vasomotor symptoms. Secondarily, data were collected to help understand the

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economic burden of vasomotor symptoms, in terms of usage of healthcare resources, number of women seeking medical care, and the number of women receiving drug therapy [18]

Methods

Study design

A cross-sectional survey was conducted in a sample of peri- and postmenopausal women living in Mexico, with ages between 40 and 65, who experienced moderate to severe menopause-related vasomotor symptoms. ISN Registration: 2693-MA-3235. This survey corresponds to a sub-analysis of the study published by Todorova et al. [19] (NCT05083884 clinical trial). An active panel was used to contact women, to identify participants as perimenopausal or postmenopausal, and to identify their vasomotor symptoms as moderate or severe.

Study population

Inclusion criteria

Women aged 40 to 65 years were sourced from the national panels of a data collection company, as elucidated in the study by Todorova et al. [19]. Each participant actively consented and successfully completed a screening questionnaire as prerequisites for inclusion in the study.

Exclusion criteria

Women currently in treatment for breast cancer, those treated with estrogen blockers, aromatase inhibitors or gonadotropin releasing hormone (GnRH) agonists / antagonists for cancer or any other activity in the last 12 months [20].

Recorded variables

Patient demographic and clinical characteristics; severity of menopause-related vasomotor symptoms (overall); number of visits to primary care and different types of specialized healthcare professionals (to estimate the economic burden of menopause-related vasomotor symptoms by collecting data from the survey and calculating out-of-pocket expenses); Number of women seeking medical advice and receiving drug treatment, and women's attitudes towards currently available treatments, as well as their role in the decision-making process.

Used questionnaires

Quality of life

For this study we used the MenQoL in its four specific domains to assess wellbeing (vasomotor; psychosocial; physical; sexual). Each item assesses the impact of one of four domains of menopausal symptoms, as experienced over the last week: vasomotor (items 1–3), psychosocial (items 4–10), physical (items 11–26), and sexual (items 27–29) [21].

Work productivity

Determined using the Work Productivity and Activity Impairment (WPAI) scale in its four domains, assessing work productivity and deterioration in activity over the past week: absenteeism (employed people missing time from work), presenteeism (reduced performance while at work) and employment status change (reduced routine working hours through changing or even losing jobs) [22].

Sleep alterations

Determined using the PROMIS instrument, which assesses self-reported perceptions on quality of sleep, depth of sleep, and sleep-associated restoration. The 8-item PROMIS Sleep-Related Impairment questionnaire (v. 1.0; 8b) measured self-reported alertness, sleepiness, tiredness, and functional impairments associated with sleep problems during waking hours within the past seven days [23].

Statistical analysis

Statistical analysis was performed with the GraphPad Prism 8.0.1 software (La Jolla, CA, USA). Qualitative variables were expressed as absolute frequencies and percentages, and continuous variables as means and standard deviations, or as medians and interquartile ranges (p75-p25), depending on the normality of data distribution. For all calculations, a p value of < 0.05 was considered as statistically significant.

Results

As shown in Figure 1, the panel contacted 7,728 women, of whom only 2,875 met the inclusion criteria, while 1,178 abandoned the study. Of the 1,697 selected women, 412 completed the survey, 12.4% of which were perimenopausal (n=51), and the remaining 87.6% were postmenopausal (n=361). Participant characteristics are described in Table 1.

The survey found that the prevalence of moderate to severe vasomotor symptoms was 16.9% (n=61) out of 361 postmenopausal women. Figure 2 shows that most surveyed women presented with more than 3 menopause-associated symptoms in the last month (>80% in both perimenopausal and postmenopausal groups). A 64.8% of the postmenopausal women were actively working (n=234/361). Results of the Work Productivity and Activity Impairment (WPAI) tool indicated that 5.9% of women missed work due to symptoms (3 or more; n=14). A larger percentage (31.6%; n=74) experienced impairment of work productivity.

Figure 1. Participant flow.

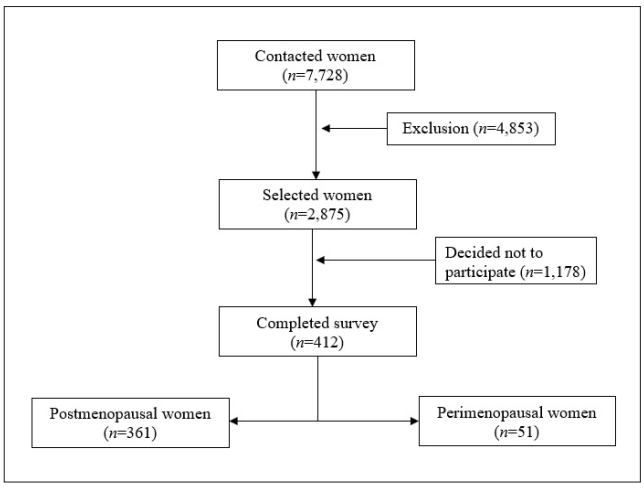


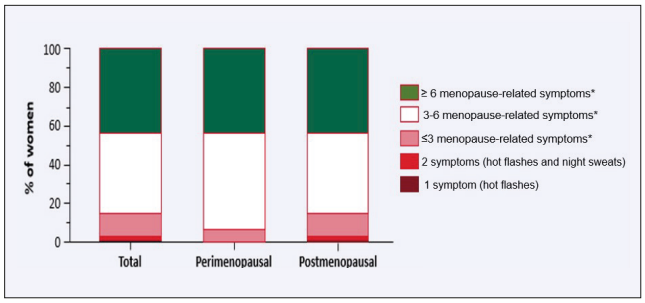
Table 1. Personal characteristics of surveyed women, grouped by peri- or postmenopausal status.

	All ***n=412***	**Perimenopausal** ***n=51***	**Postmenopausal** ***n=361***
Age range			
<40 years	0 (0)	0 (0)	0 (0)
(40-44 years)	26 (6.3)	17 (33.3)	9 (2.5)
(45-50 years)	134 (32.5)	21 (41.1)	113 (31.3)
(51-55 years)	186 (45.1)	12 (23.5)	174 (48.2)
(56-60 years)	52 (12.6)	1 (2.0)	51 (14.1)
(61-65 years)	14 (3.4)	0 (0)	14 (3.9)
Personal history			
Normal weight	111 (26.9)	10 (19.6)	101 (28.0)
Overweight	234 (56.8)	39 (76.5)	195 (54.0)
Obese	59 (14.3)	2 (3.9)	57 (15.8)
Genital bleeding with no apparent cause	13 (3.2)	4 (7.8)	9 (2.5)
Endometriosis	40 (9.7)	4 (7.8)	36 (10.0)
History of liver disease	7 (1.7)	1 (2.0)	6 (1.7)
Deep vein thrombosis	7 (1.7)	0 (0)	7 (1.9)
History of cervical cancer	6 (1.5)	0 (0)	6 (1.7)
History of ovarian cancer	6 (1.5)	0 (0)	6 (1.7)
Uterine myoma	121 (29.4)	12 (23.5)	109 (30.2)
Heart disease	4 (1.0)	0 (0)	4 (1.1)
Rheumatoid arthritis	26 (6.3)	1 (2.0)	25 (6.9)
Systemic lupus erythematosus	3 (0.7)	0 (0)	3 (0.8)
High cholesterol	143 (34.7)	10 (19.6)	133 (36.8)
Migraine	128 (31.1)	25 (49.0)	103 (28.5)
Glaucoma	5 (1.2)	0 (0)	5 (1.4)
Diabetes	77 (18.7)	4 (7.8)	73 (20.2)
Hypertension	121 (29.4)	16 (31.4)	105 (29.0)
Current smoker	76 (18.4)	16 (31.4)	60 (16.6)
Quit smoking <12 months ago	35 (8.5)	7 (13.8)	28 (7.7)
Quit smoking >12 months ago	64 (15.5)	6 (11.8)	58 (16.0)
Never smoked	237 (57.5)	22 (43.1)	215 (59.5)
Drinks alcohol	66 (16.0)	12 (23.5)	54 (15.0)
Educational level			
Elementary	3 (0.7)	0 (0)	3 (0.8)
Middle school	42 (10.2)	4 (7.8)	38 (10.5)
High school	140 (34)	13 (25.5)	127 (35.2)
College Graduate	204 (49.5)	32 (62.7)	172 (47.6)
Post-graduate	23 (5.6)	2 (3.9)	21 (5.8)
Employment status			
Employed Full-time	171 (41.5)	32 (62.7)	139 (38.5)
Employed Part-time	41 (10.0)	7 (13.7)	34 (9.4)
Self-employed	94 (22.8)	7 (13.7)	87 (24.1)
Unemployed seeking job	25 (6.1)	2 (3.9)	23 (6.4)
Unemployed not seeking job	50 (12.1)	3 (5.9)	47 (13.0)
Retired	25 (6.1)	0 (0)	25 (6.9)

Data are presented as frequencies n (%).

Lastly, the overall impact on impairment of non-work-related activities was determined across the entire studied population (*n*=412) and vasomotor symptoms were estimated to affect 35.7% of women (*n*=147) (Table 2).

Figure 2. Percentage of women presenting with menopause-related symptoms, grouped by peri- or postmenopausal status..



* % presenting in the prior month before the survey.

Table 2. WPAI questionnaire in postmenopausal women.

	n	Mean	Standard deviation
Work absenteeism	234	5.65	0.31
Impairment of work	234	29.04	0.31
Impairment of overall activity	412	34.74	0.31

Variables affecting the quality of life of peri- and postmenopausal women were recorded (Table 3a). Results from the MeNQoL quality of life questionnaire in menopausal women showed an overall score of 4.72 ± 2.5 out of 8 (with higher scores indicating a higher negative impact). Table 3b shows the scores for each of the dimensions.

Lastly, sleep quality was determined in peri- and postmenopausal women, showing that 25.9 ± 6.9% of women reported trouble sleeping. Table 4 shows the analysis of each item in the PROMIS scale.

Results showed that out-of-pocket expenses for patients were 1,261 ± 1,136 Mexican pesos over the 3 months prior to the survey. Most surveyed women considered this to be a major expense.

Around 78.4% of the 361 postmenopausal women presenting with moderate to severe vasomotor symptoms sought medical care, and 27.5% had prior medical appointments at least once a month. Of women seeking medical care, 42.1%, 47.4%, and 8.6% visited a specialist, a general practitioner, or an alternative physician, respectively. In the case of women not seeking medical advice, the survey reported that the reason for this was their refusal to take any treatment, especially hormones.

Currently, over half of surveyed women are on some type of treatment: 9.7% on hormone therapy, 3% on bio-identical hormones, 6.6% on non-hormonal therapy, 17.5% on alternative medicine and 34.9% on supplements (i.e. vitamins/calcium).

Discussion

The findings of this survey conducted in the Mexican population show that a relevant proportion of women aged 40 to 65 experience moderate to severe vasomotor symptoms. Prevalence of vasomotor symptoms in our postmenopausal Mexican women reached 17%, which aligns with the prevalence observed in Japanese women (16%), but it is notably inferior to the prevalence observed in European (40%) and US (34%) women [24].

A National Climacteric Survey conducted by the Mexican Association for the Study of Climacteric, focusing on women seeking consultation for symptoms related to the menopausal period, particularly highlighting vasomotor symptoms, revealed a range of prevalent issues. The identified symptoms including physical and mental fatigue (61.0%), irritability (54.2%), depressive mood (54.2%), sleep alterations (53.3%), and joint and muscle discomfort (52.8%) [3].

The most common barriers reported for the use of menopausal hormone therapy (MHT) are fear of increased risk of breast cancer or cardiovascular events, especially in women with a family history of these conditions. In this regard, our results are in line with previously described studies, which also show the presence of these barriers [25,26].

In the present study, women reported a wide range of psychological and physical symptoms in addition to vasomotor events, primarily, feeling tired or worn out (overall: 85% and 84.2% among postmenopausal). Lack of energy was another relevant symptom (reported by 79.8% of postmenopausal women and 80.3% overall), and difficulty sleeping was considered highly troublesome. The SWAN study also reported robust associations between vasomotor symptoms and perceived sleep disorders [27].

Of the surveyed postmenopausal women of our study, 82.8% experienced hot flashes, while 71.7% had night sweats and 84.1% experienced profuse perspiration. A 64.82% of women participants in the study were actively working. Night sweats and hot flashes had a higher impact on daily activities (34.74%) than on work activities (29.04%) [28].

Use of MHT has decreased significantly both in European countries and in the US since the publication of the results of the "Women's Health Initiative" study, which rose doubts regarding some issues related to the long-term safety of these treatments [29-31]. However, according to the NAMS/IMS guidelines, the optimal safety profile for hormone therapy is observed when initiated in healthy women under the age of 60 or within 10 years of menopausal onset. Consequently, the initiation of hormone therapy in menopausal women aged 60 and older demands a thorough assessment of individual benefits and risks [32-35].

The main strengths of the present study are given by its breadth and the diversity of assessed variables, including the use of validated questionnaires such as the MeNQoL and WPAI.

Conclusions

A proportion of women experience moderate to severe vasomotor symptoms in Mexico. Associated symptoms, such as feeling tired or worn out and sleep-related problems have an impact

Table 3. Quality of life questionnaire results: a) Overall responses on symptoms experienced in the week prior to filling the questionnaire, grouped by peri- or postmenopausal status and b) Responses by domain in postmenopausal women.

Table 3a

Symptoms	**All** ***n=412***	**Perimenopausal** ***n=51***	**Postmenopausal** ***n=361***
Hot flashes	339 (82.3)	41 (80.4)	298 (82.8)
Night sweats	300 (72.8)	41 (80.4)	259 (71.7)
Profuse perspiration	343 (83.2)	41 (80.4)	302 (84.1)
Dissatisfaction with personal life	200 (48.5)	27 (52.9)	173 (47.9)
Anxiety or nervousness	274 (66.5)	34 (68)	240 (66.7)
Poor memory	265 (64.0)	32 (62.7)	233 (64.9)
Accomplishing less than I used to	280 (68.0)	39 (76.5)	241 (66.9)
Feeling depressed, down or blue	272 (66.0)	33 (64.7)	239 (66.2)
Being impatient with other people	286 (69.4)	37 (72.5)	249 (69.2)
Feelings of wanting to be alone	268 (65.0)	38 (74.5)	230 (63.7)
Flatulence or gas pains	286 (69.4)	35 (68.6)	251 (69.7)
Joint and muscle aches	305 (74.0)	34 (66.7)	271 (75.3)
Feeling tired or worn out	350 (85.0)	47 (92.2)	303 (84.2)
Difficulty sleeping	291 (70.6)	41 (80.4)	250 (69.3)
Aches in back of neck or head	281 (68.2)	42 (82.4)	239 (67.1)
Reduced physical strength	288 (69.9)	33 (64.7)	255 (71)
Reduced stamina	291 (70.6)	31 (60.8)	260 (72.6)
Lack of energy	331 (80.3)	43 (84.3)	288 (79.8)
Dry skin	290 (70.4)	33 (66)	257 (71.2)
Weight gain	282 (68.6)	36 (70.6)	246 (68.3)
Increased facial hair	96 (23.3)	12 (23.5)	84 (23.3)
Changes in appearance, texture or tone of the skin	207 (50.2)	31 (60.8)	176 (48.8)
Feeling bloated	311 (75.5)	40 (78.4)	271 (75.1)
Low back pain	276 (67)	35 (68.6)	241 (66.8)
Frequent urination	237 (57.5)	34 (66.7)	203 (56.2)
Involuntary urination when laughing or coughing	255 (62)	29 (56.9)	226 (62.8)
Reduced sexual desire	141 (34.3)	19 (37.3)	122 (33.9)
Vaginal dryness	255 (62.2)	28 (54.9)	227 (63.2)
Avoiding intimacy	216 (52.7)	27 (52.9)	189 (52.6)

Table 3b

MenQoL subscale	***n***	**Mean**	**Standard deviation**
Vasomotor (MeNQoL items: 1 to 3)	356	5.15	2.04
Psychosocial (MeNQoL Items: 4 to 10)	351	4.56	1.94
Physical (MeNQOL Items: 11 to 26)	331	4.85	1.54
Sexual (MeNQOL Items: 26 to 29)	353	4.33	2.50
Data are presented as frequencies *n (%),* or mean and standard deviations.			

Table 4. Sleep quality questionnaire results grouped by peri- or postmenopausal status; all variables or symptoms refer to the week prior to the questionnaire.

	Total	Perimenopausal	Postmenopausal
My sleep was restless	3.28 ± 1.18	3.45 ± 1.17	3.26 ± 1.18
I was satisfied with my sleep	2.6 ± 1.15	2.35 ± 1.15	2.64 ± 1.14
My sleep was refreshing	2.5 ± 1.03	2.14 ± 0.83	2.55 ± 1.05
I had difficulty falling asleep	3.07 ± 1.34	3.35 ± 1.21	3.03 ± 1.35
I had trouble staying asleep	3.15 ± 1.11	3.29 ± 1.03	3.12 ± 1.12
I got enough sleep	2.75 ± 1.01	2.51 ± 0.9	2.79 ± 1.02
My sleep quality was good	2.9 ± 0.98	2.63 ± 0.77	2.94 ± 1.0
Data are presented as mean and standard deviations.			

on the quality of life of women and can impose a significant burden. Given that not all women presenting with moderate to severe vasomotor symptoms actively seek medical attention, telephone panel surveys offer a more robust approximation compared to surveys administered in hospitals or health units which may underestimate the prevalence of vasomotor symptoms. For women currently unable or unwilling to receive MHT, the availability of new treatment options could help improve the management of their vasomotor symptoms.

References

1. Arias E. United States life tables, 2002. Natl Vital Stat Rep. 2004;53(6):1-38.
2. Asociación Mexicana para el Estudio del Climaterio en el año 2010. Estudio y tratamiento de mujeres en el climaterio y la posmenopausia. Punto de vista de la Asociación Mexicana para el Estudio del Climaterio en el año 2010. [Study and treatment of women in the climacteric and postmenopause. Point of view of the Mexican Association for the Study of Climacteric 2010]. Ginecol Obstet Mex. 2010;78(8):423-440.
3. Legorreta D, Montaño JA, Hernández I, Salinas C, Hernández-Bueno JA; AMEC Research Committee. Age at menopause, motives for consultation and symptoms reported by 40-59-year-old Mexican women. Climacteric. 2013;16(4):417-25.
4. Santoro N, Roeca C, Peters BA, Neal-Perry G. The Menopause Transition: Signs, Symptoms, and Management Options. J Clin Endocrinol Metab. 2021;106(1):1-15.
5. Carranza-Lira S, Sandoval-Hernández CI. [Comparación de la frecuencia y magnitud de los síntomas vasomotores en mujeres pre y posmenopáusicas de la Ciudad de México]. Ginecol Obstet Mex. 2013;81(3):127-32.
6. Palacios S, Henderson VW, Siseles N, Tan D, Villaseca P. Age of menopause and impact of climacteric symptoms by geographical region. Climacteric. 2010;13(5):419-28.
7. Sievert LL, Obermeyer CM, Price K. Determinants of hot flashes and night sweats. Ann Hum Biol. 2006;33(1):4-16.
8. Gonzales GF, Villena A. Low pulse oxygen saturation in post-menopausal women at high altitude is related to a high serum testosterone/estradiol ratio. Int J Gynaecol Obstet. 2000;71(2):147-154.
9. Ortega-Ceballos PA, Morán C, Blanco-Muñoz J, Yunes-Díaz E, Castañeda-Iñiguez MS, Salmerón J. Reproductive and lifestyle factors associated with early menopause in Mexican women. Salud Publica Mex. 2006;48(4):300-307.
10. Gold EB, Colvin A, Avis N, et al. Longitudinal analysis of the association between vasomotor symptoms and race/ethnicity across the menopausal transition: study of women's health across the nation. Am J Public Health. 2006;96(7):1226-1235.
11. Freeman EW, Sammel MD, Sanders RJ. Risk of long-term hot flashes after natural menopause: evidence from the Penn Ovarian Aging Study cohort. Menopause. 2014;21(9):924-32.
12. Avis NE, Crawford SL, Greendale G, et al. Study of Women's Health Across the Nation. Duration of menopausal vasomotor symptoms over the menopause transition. JAMA Intern Med. 2015;175(4):531-539.
13. Freeman EW, Sammel MD, Lin H, Liu Z, Gracia CR. Duration of menopausal hot flushes and associated risk factors. Obstet Gynecol. 2011;117(5):1095-1104.
14. Whiteley J, Wagner JS, Bushmakin A, Kopenhafer L, Dibonaventura M, Racketa J. Impact of the severity of vasomotor symptoms on health status, resource use, and productivity. Menopause 2013;20(5): 518-524..
15. Thurston RC, Joffe H. Vasomotor symptoms and menopause: findings from the Study of Women's Health across the Nation. Obstet Gynecol Clin North Am. 2011;38(3):489-501.
16. Utian WH. Psychosocial and socioeconomic burden of vasomotor symptoms in menopause: a comprehensive review. Health Qual Life Outcomes. 2005;3:47.
17. Burleson MH, Todd M, Trevathan WR. Daily vasomotor symptoms, sleep problems, and mood: using daily data to evaluate the domino hypothesis in middle-aged women. Menopause 2010;17(1):87-95.
18. Williams RE, Kalilani L, DiBenedetti DB, Zhou X, Fehnel SE, Clark RV. Healthcare seeking and treatment for menopausal symptoms in the United States. Maturitas. 2007;58(4):348-58
19. Todorova L, Bonassi R, Guerrero Carreño FJ, et al. Prevalence and impact of vasomotor symptoms due to menopause among women in Brazil, Canada, Mexico, and Nordic Europe: a cross-sectional survey. Menopause. 2023;30(12):1179-1189.
20. Food and Drug Administration. Estrogen and Estrogen/Progestin Drug Products to Treat Vasomotor Symptoms and Vulvar and Vaginal Atrophy Symptoms — Recommendations for Clinical Evaluation. 2003. Available at: https://www.fda.gov/media/71359/download
21. Hilditch JR, Lewis J, Peter A, et al. A menopause-specific quality of life questionnaire: development and psychometric properties. Maturitas. 1996;24(3):161-175.
22. Goodman NF, Cobin RH, Ginzburg SB, Katz IA, Woode DE; American Association of Clinical Endocrinologists. American Association of Clinical Endocrinologists Medical Guidelines for Clinical Practice for the diagnosis and treatment of menopause. Endocr Pract. 2011;17 Suppl 6:1-25.
23. Varela N, Guillén-Grima F, Pérez-Cajaraville JJ, Pérez-Hernández C, Monedero P. Valoración de la repercusión del dolor sobre la productividad laboral: validación del cuestionario WPAI: Pain [Assessment of the impact of pain on work productivity: validation of the Spanish WPAI: Pain questionnaire]. An Sist Sanit Navar. 2016;39(1):77-85.

24. Nappi RE, Kroll R, Siddiqui E, et. al. Global cross-sectional survey of women with vasomotor symptoms associated with menopause: prevalence and quality of life burden. Menopause. 2021;28(8):875-882.
25. Williams RE, Kalilani L, DiBenedetti DB, et al. Frequency and severity of vasomotor symptoms among peri- and postmenopausal women in the United States. Climacteric. 2008;11(1):32-43.
26. Parish SJ, Nappi RE, Kingsberg S. Perspectives on counseling patients about menopausal hormone therapy: strategies in a complex data environment. Menopause. 2018;25(8):937-949.
27. Kravitz HM, Zhao X, Bromberger JT, et al. Sleep disturbance during the menopausal transition in a multi-ethnic community sample of women. Sleep. 2008;31(7):979-990.
28. Sarrel P, Portman D, Lefebvre P, et al. Incremental direct and indirect costs of untreated vasomotor symptoms. Menopause. 2015;22(3):260-266.
29. Pinkerton JV. Money talks: untreated hot flashes cost women, the workplace, and society. Menopause. 2015;22(3):254-255.
30. Ameye L, Antoine C, Paesmans M, de Azambuja E, Rozenberg S. Menopausal hormone therapy use in 17 European countries during the last decade. Maturitas. 2014;79(3):287-291.
31. Crawford SL, Crandall CJ, Derby CA, et al. Menopausal hormone therapy trends before versus after 2002: impact of the Women's Health Initiative Study Results. Menopause. 21;26(6):588-597.
32. Sprague BL, Trentham-Dietz A, Cronin KA. A sustained decline in postmenopausal hormone use: results from the National Health and Nutrition Examination Survey, 1999-2010. Obstet Gynecol. 2012;120(3):595-603.
33. Stuenkel CA, Davis SR, Gompel A, et al. Treatment of Symptoms of the Menopause: An Endocrine Society Clinical Practice Guideline. J Clin Endocrinol Metab. 2015;100(11):3975-4011.
34. ACOG Practice Bulletin No. 141: management of menopausal symptoms. Obstet Gynecol. 2014.;123(1):202-216.
35. de Villiers TJ, Hall JE, Pinkerton JV, et al. Revised global consensus statement on menopausal hormone therapy. Maturitas. 2016;91:153-155.

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For the Astellas criteria on data sharing see: https://clinicalstudydatarequest.com/Study-Sponsors/Study-Sponsors-Astellas.aspx