



RESEARCH ARTICLE

Hot flashes: a potential marker of deterioration of health-related quality of life

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ABSTRACT

Objective: Hot flashes are among the most common symptoms of the menopausal transition and have traditionally been considered benign and self-limiting. However, increasing evidence suggests that they may indicate broader neurovascular and inflammatory dysregulation linked to reproductive aging. The possible effect of hot flush severity on health-related quality of life (HRQoL) remains inadequately studied, particularly in Latin American populations. This study aimed to examine the association between hot flash severity and HRQoL in middle-aged women using validated tools and a large, multicenter sample.

Method: A cross-sectional study was conducted between June 2024 and January 2025 in 30 healthcare centers across 12 Latin American countries. A total of 3523 women aged 40–60 years were assessed using the Menopause Rating Scale (MRS) to evaluate vasomotor symptoms and the Short Form-36 Health Survey (SF-36) to measure HRQoL. Multivariable logistic regression models were utilized to estimate the association between hot flush severity and low HRQoL, adjusting for sociodemographic, behavioral and clinical covariates.

Results: Increasing severity of hot flushes was significantly associated with lower HRQoL scores across all SF-36 domains. In the logistic regression analysis, mild hot flushes (MRS item 1 score = 1) were associated with increased odds of impaired HRQoL (odds ratio [OR] 1.29; 95% confidence interval [CI]: 1.08–1.55), whereas very severe symptoms (MRS item 1 score = 4) demonstrated a substantially stronger association (OR 4.10; 95% CI: 2.93–5.74). Additional factors significantly associated with lower HRQoL included physical inactivity, the presence of comorbidities, obesity, current use of psychotropic medication, age ≥ 50 years and having two or more children.

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Conclusion: Hot flush severity is a strong and independent determinant of HRQoL in midlife women. These findings underscore the need for systematic assessment and targeted management of vasomotor symptoms in routine care, supporting the hypothesis that hot flashes may be a clinical marker of systemic aging.

PLAIN LANGUAGE SUMMARY

Hot flashes are one of the most common symptoms that women experience during midlife. They are often regarded as a temporary and harmless symptom. However, updated research indicates that frequent or severe hot flashes could signal broader changes in the body, impacting blood vessels, the brain and aging. In the present study, more than 3500 women (aged 40–60 years) from 12 Latin American countries participated. They completed questionnaires that assessed hot flash severity and their health-related quality of life (HRQoL) in domains such as physical health, emotional well-being, energy and daily activities. We found that women experiencing more severe hot flashes were significantly more likely to report a lower HRQoL, even after considering confounding factors such as age, body mass index, medical conditions and lifestyle. Severe hot flashes nearly doubled the likelihood of poor HRQoL. Conversely, women currently using menopausal hormone therapy had a reduced risk of poor HRQoL. These findings indicate that hot flashes are not only unpleasant but can also significantly affect women's health and everyday life. Healthcare professionals should pay close attention to hot flashes and assist women in finding effective management strategies, as they may also signal overall aging and health concerns.

Introduction

Menopause is a pivotal event in a woman's life, marked by a series of endocrine, neurobiological and psychosocial changes that significantly impact her overall health and perception of well-being [1]. Hot flashes are among the most common and characteristic symptoms occurring during and after the menopausal transition, affecting, at moderate to severe levels, 40%, 34% and 16% of women aged 40–65 years in Europe, the USA and Japan, respectively [2]. In Latin America, a study analyzing 8373 women aged 40–59 years across 12 countries found a prevalence of hot flashes of 54.5% [3]. Although traditionally considered a bothersome yet benign symptom, emerging evidence suggests that hot flashes are the clinical manifestation of complex pathophysiological changes that extend beyond the central nervous system and potentially exert significant multisystemic and functional effects [4].

From a pathophysiological perspective, hot flashes stem from a thermoregulatory disruption caused by instability in the hypothalamic thermoregulatory center. The decline in estrogen disrupts hypothalamic thermoregulation through alterations in 5-HT_{2A} and 5-HT_{1A} receptor activity and activation of the neurokinin B (HT-modulin) pathway within KNDy neurons [5]. This neuroendocrine network is further modulated by external and behavioral factors, including tobacco use, psychological stress, ambient temperature fluctuations and emotional stimuli such as fear, all of which contribute to increased vasomotor instability. From a psychological perspective, cognitive and emotional processes may amplify autonomic reactivity and sustain activation of the hypothalamic–pituitary–adrenal axis, and thereby increase the frequency and intensity of hot flashes. Additionally, obesity, psychotropic medication use, sedentary behavior and medical comorbidities – including hypertension, diabetes and cardiovascular disease – may further influence thermoregulatory and neuroendocrine responses, contributing to the persistence and severity of vasomotor symptoms [6]. However, these central mechanisms do not fully account for the extent

and severity of the phenomenon, particularly in women who experience persistent or severe hot flashes several years after menopause [7].

Hot flashes should be understood not merely as a vasomotor symptom, but as a warning sign of the systemic neuroendocrine changes that accompany reproductive aging, which may affect multiple organs and functions. For example, women experiencing more intense or frequent hot flashes tend to have a higher prevalence of central obesity, disturbances in lipid metabolism, increased inflammatory marker levels, raised blood pressure and a greater risk of developing insulin resistance [8]. Furthermore, studies have correlated hot flashes with more significant loss of bone mineral density, onset of sleep disorders, chronic fatigue, anxiety, depressive symptoms and mild cognitive impairment [9–11]. In this context, hot flashes may be viewed as a clinical marker of neurovascular and inflammatory dysfunction with potential implications for overall women's health.

Health-related quality of life (HRQoL) is a multidimensional concept that assesses an individual's subjective perception of how their physical, emotional and social health affects their overall well-being and functioning [12]. In recent decades, this concept has gained increasing importance in clinical research, as it highlights aspects of health that might not be visible through traditional biomedical measures. For menopausal women, HRQoL can be affected by many interconnected factors, such as vasomotor symptoms, sleep disturbances, changes in body image, reduced sexual desire, and shifts in social and family roles [13]. Severe or persistent hot flashes can disrupt daily activities, work performance, personal relationships and emotional well-being, ultimately reducing perceived health and overall quality of life [14].

Although extensive literature documents the prevalence of hot flashes and their impact across various health areas, few studies have systematically examined the connection between hot flush severity and HRQoL using validated tools. This gap is significant in primary care environments and among middle-aged groups, where menopausal symptoms are often

underdiagnosed or undervalued. Additionally, many previous studies have relied on generic or inadequately sensitive instruments used to assess women's subjective experiences during the menopausal transition [15].

Recognizing the aforementioned impact of hot flashes over HRQoL, it is reasonable to hypothesize that women experiencing more severe hot flashes perceive their health less positively, face greater disruption to daily activities and carry a higher emotional burden related to their menopausal status. However, to establish a measurable link, it is necessary to use specific and validated tools that quantify both symptom severity and its effect on everyday life. Therefore, the aim of the present study was to investigate the relationship between the severity of hot flashes and HRQoL in middle-aged women, utilizing internationally validated tools adapted for local populations.

The central hypothesis of this research was that severe hot flashes are independently linked to a significant decline in HRQoL in middle-aged women.

Methods

Study design and participants

This cross-sectional study was conducted between June 2024 and January 2025 across 30 healthcare centers in 12 Latin American countries: Argentina, Bolivia, Brazil, Chile, Colombia, Costa Rica, Ecuador, Mexico, Panama, Paraguay, Peru and the Dominican Republic.

Participants were women aged 40–60 years who were native speakers of Spanish or Portuguese (in the case of Brazil), attending routine gynecological consultations and self-reporting as being in good health. Good health was defined as the absence of clinically manifest diseases or disorders, along with an appropriate level of physical, mental and social functioning for their age and social context, enabling them to carry out daily activities without significant limitations. Women were excluded if they had undergone chemotherapy or radiotherapy, had a history of bilateral oophorectomy, experienced menopause before the age of 40 years, had a body mass index below 18.5 kg/m², or showed hearing or visual impairments. Women diagnosed with dementia, which could impair their ability to understand the questionnaires, were also excluded. For the purpose of this study, women were assessed for general data, menopausal symptoms and HRQoL.

Studied variables

Sociodemographic and general health variables

A range of sociodemographic, gynecological and general health variables were collected and analyzed. These included age (years), educational level (years of formal schooling) and anthropometric measures such as weight (kilograms), height (meters) and body mass index, calculated as weight divided by height squared (kilograms per square meter). Concerning reproductive history and sexual activity, the variables considered were parity (total number of children), partnership status

(presence or absence of a stable partner) and recent sexual activity, defined as having had at least one sexual intercourse in the past year (yes/no). Additionally, data were recorded on current use of menopausal hormone therapy (MHT) (yes/no).

Lastly, the following dichotomous variables (yes/no) were included: tobacco consumption; physical inactivity, defined as engaging in less than 150 min per week of moderate-intensity aerobic exercise (i.e. brisk walking, cycling, light sports or dancing); current use of psychotropic medication (including antidepressants, hypnotics or anxiolytics); and the presence of comorbidities, defined as having a current medical diagnosis and treatment for at least one of the conditions of dyslipidemia, diabetes mellitus or arterial hypertension.

Hot flashes

The severity of hot flashes was assessed using item 1 of the Menopause Rating Scale (MRS) on a Likert scale from 0 (not present) to 4 (very severe). Officially validated versions of the scale in Spanish and Portuguese (for Brazilian participants) language were employed to ensure linguistic and cultural appropriateness [16,17]. Given that the primary objective of the study was to examine hot flashes as clinical markers of health and their association with HRQoL, rather than outcomes according to reproductive aging stage, menopausal status based on bleeding patterns was not included in the analytical models.

Health-related quality of life

HRQoL was assessed using the Short Form-36 Health Survey (SF-36), which comprises 36 questions designed to capture all relevant aspects of an individual's health status. The questions are grouped into eight distinct domains: Physical Functioning (limitations in performing a wide range of physical activities; 10 items), Role Limitations due to Physical Health (problems with work or other daily activities due to physical health; four items), Bodily Pain (intensity of pain and its interference with normal work, both at home and outside; two items), General Health (personal perceptions of current health, future health prospects, and resistance to illness; five items), Vitality (feelings of energy and fatigue; four items), Social Functioning (extent to which physical or emotional problems interfere with social activities; two items), Role Limitations due to Emotional Problems (difficulties with work or daily activities due to emotional problems; three items) and Mental Health (general mental health, including depression, anxiety, behavioral control, and psychological wellbeing; five items). Responses use Likert scales (2, 3, 5 or 6 points). Some items are reversed so that higher scores always reflect better HRQoL. Raw responses are transformed to a 0–100 scale, with higher values indicating better HRQoL. Domain scores are calculated as the mean of all transformed item scores in that domain. The average of the eight domains scores was used as a comprehensive global measure of HRQoL.

The SF-36 has been translated and psychometrically validated for use in Spanish and Brazilian Portuguese language across Latin American populations [18,19]. Its internal consistency in the present study was assessed using Cronbach's α .

Statistical analysis

All statistical analyses were performed using Stata, version 19 (StataCorp LLC, College Station, TX, USA). Continuous variables are presented as means and standard deviations or medians [interquartile ranges], and categorical variables as absolute frequencies and percentages. Levene's test was employed to assess the homogeneity of variances (with $p > 0.05$ indicating homogeneity), and the Kolmogorov–Smirnov test was used to evaluate the normality of data distributions. Depending on these assumptions, comparisons of continuous variables were conducted using either Student's *t*-test (for normally distributed data) or the non-parametric Mann–Whitney *U*-test (for non-normal distributions). Associations between categorical variables were examined using the chi-square test, with results being reported as odds ratios (ORs) with corresponding 95% confidence intervals (CIs).

To assess the association between low HRQoL (defined as a total SF-36 score at or below the sample-wide median of 70.1%) and hot flashes, a logistic regression model was fitted to identify factors associated with poor quality of life. Categorical variables were modeled using indicator (dummy) variables, with the reference category serving as the baseline. Model assumptions and performance were systematically evaluated. Linearity of the logit for non-dichotomous predictors was assessed using LOWESS-smoothed plots, and model specification was examined using the link test. Model calibration was evaluated using the Brier score, calibration plots, and the calibration intercept and slope, while discrimination was assessed by the area under the receiver operating characteristic curve. Influential observations were examined using leverage statistics and deviance residuals, and multicollinearity was assessed using variance inflation factors and condition indices.

Ethical considerations

The study protocol of the REDLINC study was revised and approved by the Ethics Committee of the University of Cartagena (reference number 178-26-11-24-1-1), based in Cartagena, Colombia. The research was conducted in accordance with the principles outlined in the Declaration of Helsinki. Before participation, all women were fully informed about the study's aims and procedures and provided written informed consent. This article was initially written in Spanish and subsequently translated into English. Grammar and style corrections were supported by Grammarly (www.grammarly.com), an artificial intelligence-powered writing assistant.

Results

Table 1 presents the sociodemographic and clinical characteristics of participants according to hot flush intensity. Women with severe–very severe symptoms (MRS item 1 score = 3 and 4) were older (51.1 ± 4.6 vs. 49.4 ± 5.8 years; $p < 0.001$), had fewer years of education (13 [7] years; $p < 0.001$) and had more children ($p < 0.001$) compared to those without hot flashes. Current MHT use was higher in the mild group than in the asymptomatic group ($p = 0.003$), but not in the severe group ($p > 0.05$). Physical inactivity, obesity and smoking were

Table 1. Sociodemographic and clinical characteristics of participants ($n = 3523$) according to hot flash intensity.

Characteristic	Hot flashes (MRS item 1)				
	Absent (score 0)	Mild–moderate (score 1–2)		Severe (score 3–4)	
	n = 1382	n = 1566	p-Value ^a	n = 575	p-Value ^b
Age (years)	49.4 ± 5.8	50.9 ± 5.3	<0.001 ^c	51.1 ± 4.6	<0.001 ^c
Years of education	15.0 ± 4.6	14.4 ± 4.7	<0.001 ^c	13 [7]	<0.001 ^d
Number of children	2 [1]	2 [2]	<0.001 ^d	2 [2]	<0.001 ^d
Has a partner	73.4 (71.1–75.8)	75.6 (73.5–77.7)	0.178 ^e	71.8 (68.1–75.5)	0.463 ^e
Sexually active	79.2 (77.1–81.4)	77.2 (75.1–79.3)	0.183 ^e	75.8 (72.3–79.3)	0.096 ^e
Current MHT use	14.6 (12.7–16.5)	18.6 (16.7–20.6)	<0.003 ^e	15.7 (12.7–18.6)	0.558 ^e
Physical inactivity	45.1 (42.5–47.7)	50.1 (47.7–52.6)	<0.006 ^e	53.7 (49.7–57.8)	<0.001 ^e
Obesity (BMI ≥ 30 kg/m ²)	19.5 (17.4–21.6)	20.3 (18.3–22.3)	0.568 ^e	27.0 (23.3–30.6)	<0.001 ^e
Smoker	8.8 (7.3–10.3)	9.7 (8.2–11.2)	0.374 ^e	15.1 (12.2–18.1)	<0.001 ^e
Current psychotropic drug use	20.3 (18.2–22.5)	27.0 (24.8–29.2)	<0.001 ^e	39.0 (35.0–43.0)	<0.001 ^e
Presence of comorbidities	26.5 (24.2–28.8)	38.7 (36.3–41.1)	<0.001 ^e	40.7 (36.7–44.7)	<0.001 ^e

^aComparing mild–moderate versus absent.

^bComparing severe–very severe versus absent.

^cp-Value obtained using Student's *t*-test.

^dp-Value obtained using the Mann–Whitney *U*-test.

^ep-Value obtained using the chi-square test.

Data presented as mean ± standard deviation, medians [interquartile range] or percentage (95% confidence interval). Hot flush intensity was defined by the score of item 1 of the Menopause Rating Scale (MRS): 0 = absent, 1–2 = mild–moderate, 3–4 = severe–very severe. BMI, body mass index; MHT, menopausal hormone therapy.

significantly more frequent in the severe–very severe group ($p < 0.001$ for all). Use of psychotropic medication and the presence of comorbidities was also higher among women with severe–very severe hot flashes (39.0% vs. 20.3% and 40.7% vs. 26.5%, respectively; $p < 0.001$).

Table 2 summarizes the association between hot flush severity and HRQoL, as measured by the SF-36. Internal consistency of the SF-36 in this study was assessed using Cronbach's α coefficients. The values obtained for each domain were as follows: Physical Functioning ($\alpha = 0.91$), Role Limitations due to Physical Health ($\alpha = 0.89$), Bodily Pain ($\alpha = 0.78$), General Health ($\alpha = 0.72$), Vitality ($\alpha = 0.81$), Social Functioning ($\alpha = 0.61$), Role Limitations due to Emotional Problems ($\alpha = 0.84$) and Mental Health ($\alpha = 0.77$), indicating acceptable to excellent reliability across domains. A global Cronbach's α coefficient was also calculated ($\alpha = 0.94$). Nevertheless, given the multidimensional structure of the SF-36, reliability estimates at the domain level remain the most methodologically appropriate and clinically meaningful.

Across all domains, increasing hot flush severity was significantly associated with lower SF-36 domain scores (HRQoL). Women with severe–very severe hot flashes reported significantly poorer scores in Physical Functioning, Role Limitations

Table 2. SF-36 domain scores according to the intensity of hot flashes.

SF-36 domain	Hot flashes				
	Absent n=1382	Mild-moderate n=1566	p-Value ^a	Severe-very severe n=575	p-Value ^b
Physical Functioning	85.3±21.4	79.9±20.8	<0.001 ^c	80 [35]	<0.001 ^d
Role Limitations due to Physical Health	81.2±33.5	71.3±38.7	<0.001 ^c	65.4±40.9	<0.001 ^c
Bodily Pain	80 [30]	70 [30]	<0.001 ^d	61.5±24.0	0.001 ^c
General Health Perception	65 [20]	55 [25]	<0.001 ^d	50 [25]	<0.001 ^d
Vitality	61.1±18.7	55.1±18.6	<0.001 ^c	47.9±20.4	<0.001 ^c
Social Functioning	35.1±10.2	33.5±9.5	<0.001 ^c	30.3±10.2	<0.001 ^c
Role Limitations due to Emotional Problems	82.5±33.3	72.1±38.3	<0.001 ^c	63.3±42.8	<0.001 ^c
Mental Health	68.8±17.8	65.1±17.0	<0.001 ^c	59.1±18.9	<0.001 ^c
Total SF-36 score	74.5 [15.0]	69.2 [17.9]	<0.001 ^d	64.7 [20.3]	<0.001 ^d

^aComparing mild-moderate versus absent.^bComparing severe-very severe versus absent.^cp-Value obtained using Student's *t*-test.^dp-Value obtained using the Mann-Whitney *U* test.

Data presented as mean±standard deviation or median [interquartile range]. Hot flash intensity was defined by the score of item 1 of the Menopause Rating Scale (MRS): 0=absent, 1-2=mild-moderate, 3-4=severe-very severe. SF-36, Short Form Health Survey 36.

due to Physical Health and Bodily Pain, compared to asymptomatic women. Significant differences were also observed in General Health (50 [25] vs. 65 [20]; $p<0.001$), Social Functioning (30.3±10.2 vs. 35.1±10.2; $p<0.001$) and Role Limitations due to Emotional Problems (63.3±42.8 vs. 82.5±33.3; $p<0.001$). Similar results were observed in the domains of Vitality and Mental Health. Women with mild to moderate symptoms exhibited intermediate values in all these domains, which were also significantly lower than those of asymptomatic participants ($p<0.001$ for all comparisons). The overall SF-36 score declined gradually with increasing symptom severity (74.5 [15.0] in asymptomatic women versus 69.2 [17.9] in the mild-moderate group and 64.7 [20.3] in the severe-very group; $p<0.001$).

Using the covariates presented in Table 1, the study fitted a logistic regression model (Stata, version 19; StataCorp LLC) to examine the association between hot flash severity (MRS item 1 levels) and low HRQoL, adjusting for relevant covariates. Low HRQoL was defined as an overall SF-36 score at or below the sample-wide median (70.1%). This cut-off was chosen to ensure a consistent outcome definition across hot flash severity groups, enhancing comparability and minimizing bias from subgroup-specific thresholds.

The logistic regression model met all assessed assumptions and performance criteria. Linearity of the logit for hot flashes and number of children was confirmed using LOWESS-smoothed plots, and the link test showed no evidence of model misspecification. Model calibration was acceptable, with a Brier score of 0.209, a calibration intercept near 0 and a calibration slope near 1, supported by calibration plots showing close agreement between predicted and

Table 3. Multivariable logistic regression assessing the association between hot flash severity (MRS item 1) and low HRQoL, adjusted for relevant covariates.

Characteristic	Odds ratio (95% CI)
MRS item 1 (score 1)	1.29 (1.08–1.55)
MRS item 1 (score 2)	2.26 (1.84–2.76)
MRS item 1 (score 3)	2.93 (2.25–3.82)
MRS item 1 (score 4)	4.10 (2.93–5.74)
Physical inactivity	2.25 (1.94–2.60)
Presence of comorbidities	1.90 (1.62–2.23)
Obesity (BMI ≥ 30 kg/m ²)	1.57 (1.31–1.88)
Current psychotropic drug use	1.49 (1.26–1.76)
Age (≥50 years)	1.36 (1.17–1.58)
Current MHT use	1.29 (0.95–1.75)
Number of children (≥2)	1.15 (1.08–1.22)

Low HRQoL was defined as a total SF-36 score at or below the sample-wide median (70.1%). Hot flashes were entered as dummy variables according to severity: Menopause Rating Scale (MRS) item 1=1 (mild), 2 (moderate), 3 (severe) and 4 (very severe), with 0 (no hot flashes) as the reference category. BMI, body mass index; CI, confidence interval; HRQoL, health-related quality of life; MHT, menopausal hormone therapy.

observed risks. Discriminative ability was moderate (area under the curve = 0.73), appropriate for estimating associations and probabilistic risk rather than diagnostic classification. No influential observations were detected based on leverage statistics and deviance residuals, and Cook's distance was not applied, as it is not a standard diagnostic for logistic regression in Stata, version 19. Multicollinearity was negligible, with low variance inflation factors and condition indices, indicating stable coefficient estimates.

Table 3 shows a progressive increase in the odds of impaired HRQoL with increasing hot flash severity. For mild hot flashes (MRS score 1), the OR was 1.29 (95% CI: 1.08–1.55), rising to 4.10 (95% CI: 2.93–5.74) for the highest severity category (MRS score 4). Other significant predictors included physical inactivity (OR 2.25; 95% CI: 1.94–2.60), presence of comorbidities (OR 1.90; 95% CI: 1.62–2.23), obesity (OR 1.57; 95% CI: 1.31–1.88), current psychotropic drug use (OR 1.49; 95% CI: 1.26–1.76), age ≥50 years (OR 1.36; 95% CI: 1.17–1.58) and having two or more children (OR 1.15; 95% CI: 1.08–1.22). Current MHT use was retained in the model but did not reach statistical significance (OR 1.29; 95% CI: 0.95–1.75).

Discussion

The study findings show a strong and consistent link between the severity of hot flashes and reduced HRQoL in middle-aged women. Women experiencing severe and the highest severity category (MRS score 3 and 4) of hot flashes had significantly lower scores across all SF-36 domains. This observation aligns with an increasing body of evidence linking hot flashes to reduced quality of life and greater health burdens. Findings from the Study of Women's Health Across the Nation (SWAN) indicate that women experiencing hot flashes report significantly lower quality of life [20]. However, hot flashes affect not only subjective experiences but also objective health parameters, such as increased blood pressure [21], unfavorable lipid profiles [22], insulin resistance [23] and an increased risk of developing type 2 diabetes [24]. Our findings strengthen this association, with HRQoL impairments observed in all eight domains of the SF-36.

Notably, the multivariate logistic regression models showed that the severity of hot flashes independently predicts reduced HRQoL, even after adjusting for important confounding variables such as age, obesity, physical inactivity and comorbidities; although some of these were also related factors with different degrees of strength. Specifically for hot flashes, the strength of the association increased with symptom severity, indicating a positive increasing relationship consistent with previous studies. For example, reports indicated that the association between hot flashes and worst HRQoL is most evident among women experiencing more frequent vasomotor symptoms [20,25].

Among modifiable factors, physical inactivity emerged as the strongest predictor of low HRQoL (2.25; 95% CI: 1.94–2.60), confirming its vital role in midlife health. Regular physical activity has been linked not only to improved quality of life but also to a reduction in the severity of vasomotor symptoms. Both the Royal College of Obstetricians and Gynaecologists (UK) and the North American Menopause Society recommend that women be encouraged to participate in aerobic exercise as a therapeutic approach for managing hot flashes [26]. Obesity was also consistently linked to poor HRQoL, consistent with evidence that excess adiposity may worsen thermoregulatory dysfunction and intensify hot flashes [27].

The presence of multiple chronic conditions is linked to a lower HRQoL, affecting both the physical and mental components of the SF-36 [28]. In this context, it is noteworthy that a recent study from the REDLINC cohort examined the direct and indirect associations between obesity, chronic cardiovascular and respiratory diseases, chronic hypertension, diabetes mellitus, and physical activity and the severity of menopausal symptoms (MRS scores) in postmenopausal women [29]. Using generalized structural equation modeling, the authors found that obesity is strongly associated with more severe menopausal symptoms, both directly and through related chronic conditions and behavioral factors. We speculate that the impact on HRQoL arises primarily from the interplay between hot flashes (presence and intensity) and obesity, a complex relationship that warrants further investigation through longitudinal studies.

Other factors independently associated with low HRQoL included older age (≥ 50 years) and current use of psychotropic medications. As people age, their perceived health, especially physical health, tends to decline gradually. For example, one study reported that individuals aged 55 years and older had significantly lower scores across most domains of the SF-36, indicating poorer HRQoL; additionally, men consistently scored higher than women in all domains, emphasizing a gender disparity in perceived health status [30].

Interestingly, our study found that having two or more children (parity) was associated with poorer HRQoL, but only among women with mild/moderate hot flashes. This suggests that when menopausal symptoms are not very severe, other life burdens, such as childrearing and domestic responsibilities, both emotional and practical, become more prominent and may negatively impact perceived well-being. Conversely, among women with more severe menopausal symptoms, physical and emotional discomfort likely overshadow other

factors like parity. This scenario warrants further research. Consistent with our findings, another study using the SF-36 also found that having more children was negatively associated with general health, vitality and fatigue. These links may partly be explained by the increased financial strain and psychosocial demands commonly linked to larger family sizes [31].

Notably, significant differences were observed in the SF-36 mental health and vitality domains across groups defined by hot flash severity. The mental health domain captures aspects of depression, anxiety, behavioral control and overall psychological well-being. These findings are consistent with previous reports linking HRQoL to psychological well-being, highlighting that menopause can increase vulnerability to depression and anxiety [32]. Contrary to this, one study that assessed both self-reported hot flashes and physiologically measured episodes using night-time sternal skin conductance found that psychological functioning was not significantly linked to the frequency of objectively recorded hot flashes but was related to the frequency of self-reported episodes [33]. In relation to vitality, a study by Utian found that women experiencing moderate to severe hot flashes had significantly poorer scores than those without hot flashes on four of the eight SF-36 subscales, including vitality [34]. Taken together, our findings suggest that the distress caused by hot flashes affect physical, psychological and social components of HRQoL. Therefore, it is not surprising that, in our regression model, the use of psychotropic medications was associated with low HRQoL.

The protective association between MHT use and HRQoL has been widely reported. Previous evidence supports the beneficial role of MHT in alleviating menopausal symptoms and improving daily functioning and well-being. This is consistent with findings from the Women's Health Initiative (WHI) clinical trials and several large observational studies, which have demonstrated substantial reductions in vasomotor symptoms and improvements in selected quality-of-life domains among MHT users [35,36]. In our logistic regression analysis, current MHT use was not significantly associated with HRQoL as measured by the SF-36. This lack of statistical significance may reflect the generic nature of the SF-36, residual confounding by indication and the multifactorial determinants of HRQoL that extend beyond vasomotor symptom management.

Our study has several strengths worth highlighting. First, the large sample size, including participants from 12 Latin American countries, enhances the generalizability of the findings and provides valuable insights into an under-represented population. Second, the use of internationally validated and culturally adapted instruments, such as the MRS and the SF-36, ensures the reliability and comparability of the data. Third, the study employed a robust multivariable logistic regression approach, carefully adjusting for key sociodemographic, behavioral and clinical confounders, with thorough assessment of model assumptions and fit, which strengthens the internal validity of the observed associations. Additionally, the study provides both clinical and theoretical contributions by suggesting that hot flashes may function not only as symptomatic indicators but also as a potential clinical marker of chronic health conditions.

Several limitations should also be recognized. Most importantly, the cross-sectional design prevents any inference of causality, restricting conclusions to associations only. Second, relying on self-reported measures for both for flashes and HRQoL introduces potential biases, including recall bias and social desirability bias. Third, there may be a selection bias, as participants were recruited from routine gynecological consultations and women with severe health conditions were excluded. Consequently, the sample might not fully represent more vulnerable populations. Moreover, the study did not include objective biomarkers (i.e. hormonal levels, inflammatory markers or epigenetic age estimations) that could have supported the theoretical hypothesis linking hot flashes to systemic aging. Lastly, as already mentioned, although hot flashes demonstrated a significant association with HRQoL, other aspects, that mainly revolve within obesity, seem to also interplay and negatively impact HRQoL.

From a clinical perspective, our findings provide strong evidence that the severity of hot flashes is associated with lower HRQoL in women during midlife. Notably, this relationship seems to be modifiable through behavioral and therapeutic interventions. Our results emphasize the importance of routine screening for vasomotor symptoms and the adoption of personalized management strategies in clinical practice. From a theoretical perspective, our findings align with the notion that hot flashes may serve as a clinical marker of underlying inflammatory dysfunction and, consequently, biological aging. This concept is further supported by data from the WHI, which indicate that severe hot flashes are associated with accelerated epigenetic aging [37].

In conclusion, the present study demonstrates that severe–very severe hot flashes are independently linked to lower HRQoL, even after accounting for sociodemographic and clinical factors. There is a need for longitudinal studies to further explore the interactions between hot flashes and obesity and determine their independent or associative impact on HRQoL of women transiting the menopause and beyond. The study underscores the importance of routinely assessing vasomotor symptoms in clinical practice, recognizing them as distressing menopausal symptoms and potential indicators of broader health concerns. The findings indicate that severe–very severe hot flashes may signal inflammatory dysregulation, providing supporting evidence of a connection between vasomotor symptoms and accelerated biological aging. These insights highlight the need for personalized management and long-term research.

Ethical approval

The study protocol for this research was reviewed and approved by the Ethics Committee of the University of Cartagena (178-26-11-24-1-1), Cartagena, Colombia, and adheres to the principles of the Declaration of Helsinki. Before participation, all participants were informed about the aims and procedures of the study, and they provided written informed consent thereafter.

Disclosure statement

No potential conflict of interest was reported by the authors.

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Data availability statement

There are no linked research datasets for this article. The data from this study are not publicly available but can be obtained upon reasonable request for research collaboration projects from Juan E. Blümel, subject to consideration of ethical, privacy and legislative requirements.

References

- [1] Gibbons R. The menopause transition: a call for a holistic approach. *BJPsych Bull.* 2026;50(1):62–64. doi: [10.1192/bjb.2025.17](https://doi.org/10.1192/bjb.2025.17).
- [2] 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. doi: [10.1097/GME.0000000000001793](https://doi.org/10.1097/GME.0000000000001793).
- [3] Blümel JE, Chedraui P, Baron G, et al. Menopausal symptoms appear before the menopause and persist 5 years beyond: a detailed analysis of a multinational study. *Climacteric.* 2012;15(6):542–551. doi: [10.3109/13697137.2012.658462](https://doi.org/10.3109/13697137.2012.658462).
- [4] El Khoudary SR, Greendale G, Crawford SL, et al. The menopause transition and women's health at midlife: a progress report from the Study of Women's Health Across the Nation (SWAN). *Menopause.* 2019;26(10):1213–1227. doi: [10.1097/GME.0000000000001424](https://doi.org/10.1097/GME.0000000000001424).
- [5] Karim R, Dang HM, Hodis HN, et al. Association of hot flushes with ghrelin and adipokines in early versus late postmenopausal women. *Menopause.* 2020;27(5):512–518. doi: [10.1097/GME.0000000000001508](https://doi.org/10.1097/GME.0000000000001508).
- [6] Fidecicchi T, Giannini A, Chedraui P, et al. Neuroendocrine mechanisms of mood disorders during menopause transition: a narrative review and future perspectives. *Maturitas.* 2024;188:108087. doi: [10.1016/j.maturitas.2024.108087](https://doi.org/10.1016/j.maturitas.2024.108087).
- [7] Tuomikoski P, Savolainen-Peltonen H. Vasomotor symptoms and metabolic syndrome. *Maturitas.* 2017;97:61–65. doi: [10.1016/j.maturitas.2016.12.010](https://doi.org/10.1016/j.maturitas.2016.12.010).
- [8] Ozkaya E, Kahir E, Kara F, et al. Impact of hot flashes and night sweats on carotid intima-media thickness and bone mineral density among postmenopausal women. *Int J Gynaecol Obstet.* 2011;113(3):235–238. doi: [10.1016/j.ijgo.2010.12.020](https://doi.org/10.1016/j.ijgo.2010.12.020).
- [9] Maki PM, Drogos LL, Rubin LH, et al. Objective hot flashes are negatively related to verbal memory performance in midlife women. *Menopause.* 2008;15(5):848–856. doi: [10.1097/gme.0b013e31816d815e](https://doi.org/10.1097/gme.0b013e31816d815e).
- [10] Hatcher KM, Smith RL, Chiang C, et al. Nocturnal hot flashes, but not serum hormone concentrations, as a predictor of insomnia in menopausal women: results from the midlife women's health study. *J Womens Health (Larchmt).* 2023;32(1):94–101. doi: [10.1089/jwh.2021.0502](https://doi.org/10.1089/jwh.2021.0502).
- [11] Acquadro C, Berzon R, Dubois D, et al. Incorporating the patient's perspective into drug development and communication: an ad hoc task force report of the Patient-Reported Outcomes (PRO) Harmonization Group meeting at the Food and Drug Administration, February 16, 2001. *Value Health.* 2003;6(5):522–531. doi: [10.1046/j.1524-4733.2003.65309.x](https://doi.org/10.1046/j.1524-4733.2003.65309.x).
- [12] Ye L, Knox B, Hickey M. Management of menopause symptoms and quality of life during the menopause transition. *Endocrinol Metab Clin North Am.* 2022;51(4):817–836. doi: [10.1016/j.ecl.2022.04.006](https://doi.org/10.1016/j.ecl.2022.04.006).
- [13] Tserotas K, Blümel JE, Chedraui P, et al. Association of menopausal symptoms on work performance in midlife Latin American women. *Menopause.* 2025; In press. doi: [10.1097/GME.0000000000002645](https://doi.org/10.1097/GME.0000000000002645).

- [14] Alder E. The Blatt-Kupperman menopausal index: a critique. *Maturitas*. 1998;29(1):19–24. doi: [10.1016/s0378-5122\(98\)00024-3](https://doi.org/10.1016/s0378-5122(98)00024-3).
- [15] Harlow SD, Gass M, Hall JE, et al. Executive summary of the Stages of Reproductive Aging Workshop + 10: addressing the unfinished agenda of staging reproductive aging. *J Clin Endocrinol Metab*. 2012;97(4):1159–1168. doi: [10.1210/jc.2011-3362](https://doi.org/10.1210/jc.2011-3362).
- [16] Zentrum für Epidemiologie und Gesundheitsforschung (ZEG Berlin). Menopause Rating Scale in Spanish. https://zeg-berlin.de/wp-content/uploads/2017/01/MRS_Spanish.pdf.
- [17] Zentrum für Epidemiologie und Gesundheitsforschung (ZEG Berlin). Menopause Rating Scale in Portuguese (Brazil). https://zeg-berlin.de/wp-content/uploads/2017/01/MRS_Brazil.pdf.
- [18] Olivares-Tirado P. Departamento de Estudios y Desarrollo. Superintendencia de ISAPRES. Gobierno de Chile. Estado de salud de beneficiarios del sistema de Salud de Chile 2004–2005. https://www.superdesalud.gob.cl/documentacion/666/articles-1062_recurso_1.pdf.
- [19] Ciconelli RM, Ferraz MB, Santos E, et al. Translation into Portuguese and validation of the generic health status questionnaire SF-36 (Brazil SF-36). *Rev Bras Reumatologia*. 1999;39(3):143–150.
- [20] Avis NE, Colvin A, Bromberger JT, et al. Change in health-related quality of life over the menopausal transition in a multiethnic cohort of middle-aged women: study of Women's Health Across the Nation. *Menopause*. 2009;16(5):860–869. doi: [10.1097/gme.0b013e3181a3cdaf](https://doi.org/10.1097/gme.0b013e3181a3cdaf).
- [21] Jackson EA, El Khoudary SR, Crawford SL, et al. Hot flash frequency and blood pressure: data from the study of women's health across the nation. *J Womens Health (Larchmt)*. 2016;25(12):1204–1209. doi: [10.1089/jwh.2015.5670](https://doi.org/10.1089/jwh.2015.5670).
- [22] Thurston RC, El Khoudary SR, Sutton-Tyrrell K, et al. Vasomotor symptoms and lipid profiles in women transitioning through menopause. *Obstet Gynecol*. 2012;119(4):753–761. doi: [10.1097/AOG.0b013e31824a09ec](https://doi.org/10.1097/AOG.0b013e31824a09ec).
- [23] Thurston RC, El Khoudary SR, Sutton-Tyrrell K, et al. Vasomotor symptoms and insulin resistance in the study of women's health across the nation. *J Clin Endocrinol Metab*. 2012;97(10):3487–3494. doi: [10.1210/jc.2012-1410](https://doi.org/10.1210/jc.2012-1410).
- [24] Gray KE, Katon JG, LeBlanc ES, et al. Vasomotor symptom characteristics: are they risk factors for incident diabetes? *Menopause*. 2018;25(5):520–530. doi: [10.1097/GME.0000000000001033](https://doi.org/10.1097/GME.0000000000001033).
- [25] 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. doi: [10.1016/j.ogc.2011.05.006](https://doi.org/10.1016/j.ogc.2011.05.006).
- [26] Daley AJ, Stokes-Lampard HJ, Macarthur C. Exercise to reduce vasomotor and other menopausal symptoms: a review. *Maturitas*. 2009;63(3):176–180. doi: [10.1016/j.maturitas.2009.02.004](https://doi.org/10.1016/j.maturitas.2009.02.004).
- [27] Speakman JR. 3rd series. Obesity and thermoregulation. In: Aminoff MJ, Boller F, Swaab DF, editors. *Handbook of clinical neurology*. Vol. 156. Amsterdam: Elsevier; 2018. p. 431–443. doi: [10.1016/B978-0-444-63912-7.00026-6](https://doi.org/10.1016/B978-0-444-63912-7.00026-6).
- [28] Fortin M, Dubois MF, Hudon C, et al. Multimorbidity and quality of life: a closer look. *Health Qual Life Outcomes*. 2007;5(1):52. doi: [10.1186/1477-7525-5-52](https://doi.org/10.1186/1477-7525-5-52).
- [29] Aedo S, Blümel JE, Vallejo MS, et al. Unraveling the association between obesity and climacteric symptoms: a generalized structural equation modeling approach. *Menopause*. 2026;33Aug 5. (1):48–56. doi: [10.1097/GME.0000000000002620](https://doi.org/10.1097/GME.0000000000002620).
- [30] El Emrani L, Senhaji M, Bendriss A. Measuring health-related quality of life in the population of Tetouan, Morocco, by the SF-36: normative data and the influence of gender and age. *East Mediterr Health J*. 2016;22(2):133–141. doi: [10.26719/2016.22.2.133](https://doi.org/10.26719/2016.22.2.133).
- [31] Nabolsi M, Safadi R, Sun C, et al. The health-related quality of life of Syrian refugee women in their reproductive age. *PeerJ*. 2020;8:e9990. doi: [10.7717/peerj.9990](https://doi.org/10.7717/peerj.9990).
- [32] Alblooshi S, Taylor M, Gill N. Does menopause elevate the risk for developing depression and anxiety? Results from a systematic review. *Australas Psychiatry*. 2023;31(2):165–173. doi: [10.1177/10398562231165439](https://doi.org/10.1177/10398562231165439).
- [33] Thurston RC, Blumenthal JA, Babyak MA, et al. Association between hot flashes, sleep complaints, and psychological functioning among healthy menopausal women. *Int J Behav Med*. 2006;13(2):163–172. doi: [10.1207/s15327558ijbm1302_8](https://doi.org/10.1207/s15327558ijbm1302_8).
- [34] Utian WH. Psychosocial and socioeconomic burden of vasomotor symptoms in menopause: a comprehensive review. *Health Qual Life Outcomes*. 2005;3(1):47. doi: [10.1186/1477-7525-3-47](https://doi.org/10.1186/1477-7525-3-47).
- [35] Manson JE, Chlebowski RT, Stefanick ML, et al. Menopausal hormone therapy and health outcomes during the intervention and extended poststopping phases of the Women's Health Initiative randomized trials. *JAMA*. 2013;310(13):1353–1368. doi: [10.1001/jama.2013.278040](https://doi.org/10.1001/jama.2013.278040).
- [36] Santoro N, Epperson CN, Mathews SB. Menopausal symptoms and their management. *Endocrinol Metab Clin North Am*. 2015;44(3):497–515. doi: [10.1016/j.ecl.2015.05.001](https://doi.org/10.1016/j.ecl.2015.05.001).
- [37] Thurston RC, Carroll JE, Levine M, et al. Vasomotor symptoms and accelerated epigenetic aging in the Women's Health Initiative (WHI). *J Clin Endocrinol Metab*. 2020;105(4):1221–1227. doi: [10.1210/clinem/dgaa081](https://doi.org/10.1210/clinem/dgaa081).