*Menopause: The Journal of The North American Menopause Society*
Vol. 28, No. 8, pp. 000-000
DOI: 10.1097/GME.0000000000001790
© 2021 by The North American Menopause Society

## ORIGINAL STUDY

# Predictive and criterion validity of the Cervantes-SF menopause quality of life questionnaire

*Pluvio J. Coronado, MD, PhD,[1] Manuel Monroy, PhD,[2] María Fasero, MD, PhD,[3] Laura Baquedano, MD, PhD,[4] Nicolás Mendoza, MD, PhD,[5] Plácido Llaneza, MD, PhD,[6] Javier Rejas, MD, PhD,[7] Miguel A. Ruiz, PhD,[2] and and the AEEM group for the development of the Cervantes-SF scale.*

Downloaded from http://journals.lww.com/menopausejournal by BhDMf5ePHKav1zEoum1tQfN4a+kJLhEZgbsIHo4XMi0hCywCX1AWnYQp/IlQrHD3i3D0OdRyi7TvSFl4Cf3VC4/OAVpDDa8KKGKV0Ymy+78= on 05/18/2021

**Abstract**

***Objectives:*** To determine the predictive and criterion-based validity of the Cervantes-SF scale that measures the impact of menopause on Health-Related Quality of Life.

***Methods:*** We recruited a noninstitutionalized sample of peri/postmenopausal women aged 40 to 65 years, who had their last menstrual cycle 12+ months prior to inclusion in the study of the psychometric validity of the Cervantes-SF scale. Predictive validity of the scale was confirmed for various health outcome measures administered concomitantly (years of disability-free life expectancy, work productivity and impact on daily activities, economic impact arising from loss of work productivity, hours of undisturbed sleep each day, and the utilization of healthcare facilities), whilst criterion validity was determined by the likelihood of identifying a moderate-to-severe vasomotor or genital syndrome requiring specific treatment.

***Results:*** A sample of 308 peri/postmenopausal women with a mean age of 55.7 years (SD: 5.3 y) was analyzed in this study. A score >25 points on the dimension of vasomotor problems (or menopausal health) showed values of sensitivity and specificity > 80% for identifying women with moderate-severe vasomotor syndrome requiring pharmacological treatment. Predictive validity was confirmed for menopause-related health outcomes. A change of 6.7 points in the scale score, equivalent to the value of its minimal difference, is indicative of a significant increase in the degree of disability regarding work/day-to-day activities, greater economic loss due to decreased work productivity, fewer years of life expectancy without disability, fewer hours of undisturbed sleep, and more visits to the physician per year due to menopausal symptoms.

***Conclusions:*** These results confirm the criterion and predictive validity of the Cervantes-SF scale in peri/postmenopausal women.

***Key Words:*** Cervantes-SF – Health-related quality of life – Menopause – Norms.

Menopause is associated with the loss of ovarian follicular activity, and although the age of onset varies considerably, it usually occurs around the age of 50 to 52 years.[1] During this period, women experience significant physical and psychological changes that impact their health-related quality of life (HRQoL).[2,3] HRQoL

Received January 8, 2021; revised and accepted March 3, 2021.
From the [1]Women's Health Institute, San Carlos Clinic Hospital, IdISSC, Complutense University, Madrid, Spain; [2]Faculty of Psychology, Autonoma University of Madrid, Madrid, Spain; [3]Department of Obstetrics and Gynecology, Sanitas La Zarzuela Hospital, Francisco de Vitoria University, Madrid, Spain; [4]Department of Obstetrics and Gynecology, Miguel Servet Hospital, Zaragoza, Spain; [5]Department of Obstetrics and Gynecology, School of Medicine, University of Granada, Spain; [6]Department of Obstetrics and Gynecology, Central Hospital of Asturias, University of Oviedo, Spain; and [7]Department of Pharmacoeconomics and Health Outcomes Research, Pfizer SLU, Alcobendas, Madrid, Spain.
Funding/support: This work was promoted and sponsored by the Spanish Menopause Society. Statistical analyses were conducted by Manuel Monroy and Miguel Ruiz from the Universidad Autónoma de Madrid, and was funded by Pfizer, S.L.U. No editorial support was provided except for a review of the English, conducted by Your English Lab.

Financial disclosure/conflicts of interest: The AEEM group responsible for the study of the psychometric validation of the Cervantes Short-Form consists of P.J.C., Rafael Sánchez-Borrego, L.B., Sonia Sánchez, Cristina Argudo, Micaela Fernández-Abellán, Silvia González, Eva Iglesias, Jackie Calleja, Jesus Presa, Alfonso Duque, Fernando Ruiz, Borja Otero, María Fasero, Plácido Llaneza y Santiago Palacios. J.R. is an employee of Pfizer, S.L.U. M.M. and M.A.R. are professors of statistics and methodology at the Universidad Autónoma de Madrid and were responsible for the statistical analysis, which was funded by Pfizer, S.L.U. The other authors have no conflicts to declare.

Contributions: All authors had complete access to the data, participated in the analysis and/or interpretation of results, and drafted the manuscript. P.J.C., M.F., L.B., N.M., P.L., and J.R. were responsible for the design of the study. Data analyses were conducted by M.M. and M.A.R. All authors have viewed and approved the final version.

Supplemental digital content is available for this article. Direct URL citations are provided in the HTML and PDF versions of this article on the journal's Website (www.menopause.org).
Address correspondence to: Dr. Pluvio J. Coronado, MD, PhD, Instituto de Salud de la Mujer. Hospital Clínico San Carlos, C/ Prof. Martín Lagos, s/n, 28040 Madrid, Spain. E-mail: pcoronadom@gmail.com



Copyright © 2021 The North American Menopause Society. Unauthorized reproduction of this article is prohibited.

assessment has therefore become an essential component of studying the effects of menopause on well-being, as well as evaluating the benefits of hormonal treatments or any other therapy used at this stage of a woman's life.[4-6] The Cervantes scale is a self-administered, multidimensional questionnaire designed to measure HRQoL in peri- and postmenopausal women.[7] A 16-item shortened version (Cervantes-SF) of the scale has been developed (compared with the 31-item original version), which has been shown to have good psychometric properties while being more feasible to apply in daily clinical practice. In addition, the Cervantes-SF preserves the structure of the original scale with the following four first-order dimensions and three second-order dimensions[8]: Menopause and Health (Vasomotor Symptoms, Health and Aging), Psychology, Sexuality, and Partner Relationship.[9,10] This version has been shown to measure a health concept equivalent to that measured by the original Cervantes scale,[8] while being more feasible to administer and score. Although the short version of the Cervantes scale has previously been shown to have good psychometric properties, rather less is known about its other attributes such as criterion or predictive validity.

Criterion validity is a property that indicates whether this new instrument measures a concept similar to that assessed by the original scale, while predictive validity informs us of the instrument's ability to explain or predict women's health outcomes that have not been directly measured or are expected to occur in the future.[11-13] Confirmation of the criterion validity of the Cervantes-SF would allow this abridged version to be used as a substitute for the existing instrument without losing information about the women, with the added advantage of imposing a lower administration load. Establishing the predictive validity of the scale would support its use in routine clinical practice for estimating the deterioration of HRQoL resulting from menopausal symptomatology and identifying various health outcomes that could guide the decision making of both clinicians and women. Therefore, this study aimed to determine both the criterion validity of the scale for identifying menopausal symptomatology requiring pharmacological treatment, and the predictive validity of the instrument for a number of health outcomes.

## METHODS

### Study design

We conducted a cross-sectional, observational, noninterventional study, following the STROBE initiative guidelines and checklist (See Supplemental Digital Content, http://links.lww.com/MENO/A766, https://www.strobe-statement.org).[14]

### Population

The data used to test the criterion and predictive validity of the Cervantes-SF were extracted from the psychometric validation study of the Cervantes-SF scale.[9] This study initially included 317 women, although the effective sample was composed of 308 women who met the selection criteria, and was the sample used to confirm the factor structure of the scale and some of its psychometric properties. Inclusion criteria were perimenopausal or postmenopausal women according to STRAW[15] criteria, who reported having their last menstrual period 12 or more months prior to inclusion in the study, and with an age range of 40 to 65 years. All of the women had provided written consent to participate in the study. We excluded women with a regular menstrual period, a cancer diagnosis, or an uncontrolled severe health condition, along with those receiving oncological or psychopharmaceutical treatments. This study was conducted in gynecology outpatient clinics at 13 hospitals across 7 different regions of Spain. Information was collected on climacteric symptomatology, sociodemographic data and clinical history, as well as various patient-reported outcome (PRO) measures.

### Criterion validity testing

Criterion validity was checked by establishing the a priori hypothesis that the Cervantes-SF scale shows a significant relationship with the main clinical criteria used to evaluate the characteristic symptomatology of menopause.[10-13] These criteria are the presence of vasomotor (vasomotor syndrome) and genital symptoms (genital syndrome),[16] along with receiving treatment for this symptomatology, and the type of treatment applied. The Menopause Symptom Severity Scale (see Supplemental Digital Content,[17,18] http://links.lww.com/MENO/A766) was used to group women with both vasomotor and genital syndrome into the following four categories: absent, mild, moderate, and severe. We then assessed whether they were receiving pharmacological treatment, along with the type of drugs applied, which included specific treatments (menopausal hormone therapy [MHT], selective estrogen-receptor modulators, isoflavones, or black cohosh), nonspecific treatments (antidepressants, anxiolytics, or hypnotics), or both.

### Predictive validity testing

To test the predictive validity of the scale, we used a number of variables, along with the PROs included in the mentioned psychometric validation study (see Supplemental Digital Content for a description of the scales and questionnaires used, http://links.lww.com/MENO/A766).[9] The PROs included the Spanish versions of the EQ-5D-3L (EuroQoL Group)[19] and the WPAI-General Health (WPAI-GH, Work Productivity and Activity Impairment Questionnaire—General Health).[20] The variables used for evaluating predictive validity were the hours of undisturbed sleep each day (effective sleep hours),[21] and healthcare burden expressed as the monthly number of visits to family medical and gynecology clinics due to menopausal symptoms, projected on an annual basis. The EQ-5D-3L instrument was used to calculate the utility or social value that society grants to the health status of the individual, along with a complementary disutility or disability score. The disutility score was used to estimate the years of life expectancy lost due to disability, which, subtracted from the current years of life expectancy according to the age of each participant, allowed us to obtain the disability-adjusted-life-expectancy. This value is expressed


© 2021 The North American Menopause Society

Copyright © 2021 The North American Menopause Society. Unauthorized reproduction of this article is prohibited.

in years and represents, for each participant, the time of healthy life expectancy without disability (see Supplemental Digital Content, http://links.lww.com/MENO/A766).[22] The EQ-5D-3L is accompanied by a visual analog scale (EQ-VAS) that measures the women's current self-assessed health status and takes values between 0 (worst imaginable health) and 100 (best imaginable health). The WPAI-GH questionnaire was used to measure the percentage of lost work productivity (absenteeism and presenteeism) and the percentage of impairment in daily life activities resulting from a health problem.[22] By multiplying the percentage of work disability by the average net annual labor cost (in this case the last available estimate corresponds to that of the year 2018 in Spain; average= 30,883.44€; National Statistics Institute, 2018),[23] it was possible to estimate the economic loss per active person each year due to lost or decreased labor productivity.

### Statistical analysis

Statistical analyses were conducted using the IBM SPSS package, Version 26.0, NY, (https://www.ibm.com/analytics/spss-statistics-software). First, a descriptive analysis of the sociodemographic and clinical variables was conducted, along with climacteric symptomatology in those cases where this information was available. Criterion validity was initially analyzed by estimating the strength and statistical significance of the correlation between scores on the Cervantes-SF scale (total score and dimensions) and the intensity of vasomotor and genital syndromes using Pearson's r and Spearman's rho coefficients (See Supplemental Digital Content Table S1A and Table S1B, http://links.lww.com/MENO/A766). Once the existence of a significant correlation was demonstrated, the women were grouped according to the intensity of the vasomotor and genital syndromes using a dichotomous criterion: absent/mild and moderate/severe in both cases. This classification criterion was chosen because it is the one that best categorizes women according to their need for pharmacological treatment for climacteric symptoms in the analyzed sample and therefore has greater practical utility from a clinical standpoint.[24] The percentages of women receiving treatment (any, specific, nonspecific, or MHT only) for vasomotor and genital syndrome according to the above classification were calculated and binary logistic regression was used to estimate the odds ratio (with a confidence interval [CI] of 95%) as a measure of the strength of the correlation. Once it had been confirmed that the likelihood of receiving treatment is significantly higher in women with moderate-to-severe vasomotor or genital syndrome, receiver-operating-characteristic (ROC) curve analysis was used to estimate the cut-off point in the Cervantes-SF scale total score, and in each of its dimensions, which best categorizes menopausal women according to the intensity of both vasomotor and genital syndromes. Youden's J index was used to select the optimal cut-off point, calculating the combination of sensitivity and specificity indicators for each possible cut-off point.[25] The indicators of positive predictive value, negative predictive value, positive and negative likelihood ratio (LR) were also calculated. LR(+) indicates the likelihood of finding a score higher than the proposed cut-off point for criterion validity in women with a moderate/severe vasomotor or genital syndrome compared with those without; and LR(−) indicates the likelihood of finding a score lower than the proposed cut-off point for criterion validity in women with moderate/severe vasomotor or genital syndrome compared with those without.

Predictive validity was assessed by predicting several health outcomes through multivariate linear regression analysis, whilst preserving the total score of the Cervantes-SF scale as an explanatory variable, both in continuous form and clustered into normative percentiles. The stepwise elimination method was applied for the remaining independent variables proposed in the models: age (years), body mass index (kg/m$^2$), education level, marital status, menopausal status (peri or postmenopausal), age at menarche (years), number of comorbidities, and their severity according to Charlson's eight-item abbreviated severity index (0-10 points),[26] tobacco consumption (yes/no) and alcohol consumption (yes/no), and pharmacological treatment for climacteric syndrome (yes/no). The health outcomes used as criterion (or dependent) variables to test the predictive validity of the Cervantes-SF were degree of impairment in performing work and daily activities (both expressed as a percentage) measured by the WPAI-GH questionnaire, economic loss per person per year due to decreased work productivity (euros, year 2018), current self-reported health status measured by the EQ-VAS, years of healthy life expectancy without disability, daily hours of undisturbed (effective) sleep, and the number of annual medical visits due to menopausal symptoms. From the estimated models, we calculated, for each health outcome, the minimally relevant change by multiplying the β-coefficient of each health outcome by the minimally important difference (MID) of the Cervantes-SF scale. The MID is equivalent to the smallest change (both increase and decrease) in the total Cervantes-SF scale score perceived by the menopausal woman when a change in health-related quality of life has occurred due to menopausal symptoms.[27-29] In the total score of the Cervantes-SF scale, the magnitude of the MID is equivalent to one time the standard error of measurement (SEM) which is of a magnitude equal to 6.7 points in the total score of the scale, as identified during psychometric validation of the scale.[8]

## RESULTS

The original sample consisted of 317 women with a mean age of 55.7 years (SD = 5.3 y), while the effective sample size analyzed was reduced to 308 women, since 9 (2.8%) were excluded because they did not meet the selection criteria. Table 1 shows the main demographic descriptors. Most of the women (75.4%) were in the postmenopausal stage, while 22.3% were in the perimenopausal stage. Of the sample, 78.7% were sexually active and had an average body mass index of 25.2 kg/m$^2$ (SD= 4.2 kg/m$^2$), and 69% of the women regularly attended a gynecology clinic for their menopause check-up. A total of 25.6% of the women were current



Copyright © 2021 The North American Menopause Society. Unauthorized reproduction of this article is prohibited.

**TABLE 1.** *Demographic and clinical data of the women included in the psychometric validation study of the Cervantes-SF scale*

| | |
|---|---|
| Age (y): mean (SD) | 55.7 (5.3) |
| BMI (kg/m$^2$): mean (SD) | 25.2 (4.2) |
| Menopausal stage (%)[a] | |
| Postmenopausal | 232 (75.4%) |
| Perimenopausal | 69 (22.3%) |
| Sexually active: (%) | 235 (78.7%) |
| Attending menopause consultation: (%) | 213 (69.0%) |
| Climacteric symptoms: (%) | |
| Hot flashes | 228 (73.8%) |
| Decrease in sexual drive | 222 (71.8%) |
| Vaginal dryness | 217 (70.2%) |
| Sweating | 202 (65.4%) |
| Dyspareunia | 150 (48.5%) |
| Tremors | 92 (29.8%) |
| Irritability | 12 (3.9%) |
| Dysthymia | 8 (2.6%) |
| Insomnia | 7 (2.3%) |
| Asthenia | 6 (1.9%) |
| Changes in mood | 6 (1.9%) |
| Joint pain | 6 (1.9%) |
| Nervousness | 5 (1.6%) |
| None | 27 (9%) |
| Educational level (%) | |
| None | 0 (0%) |
| Primary | 56 (18%) |
| Secondary | 108 (35%) |
| Professional degree | 1 (0.3%) |
| Higher | 142 (17%) |
| Employment status (%) | |
| Active | 216 (70%) |
| Disabled | 4 (1%) |
| Unemployed | 16 (5%) |
| Retired | 11 (4%) |
| Homemaker | 57 (19%) |
| Civil status (%) | |
| Single | 25 (8%) |
| Married | 221 (72%) |
| Divorced | 42 (14%) |
| Widowed | 18 (6%) |
| Other | 2 (1%) |
| Smoker (%) | 78 (25.6%) |
| Cigarettes (units/day): mean (SD) | 10.3 (5.5) |
| Alcohol consumption (%) | 77 (25.2%) |
| Units/day: mean (SD) | 1.2 (0.5) |

Some patients did not respond to all questions on the case record form. Climacteric symptoms may total more than 100%.
BMI, body mass index; SD, standard deviation.
[a]For seven of the women, the menopausal stage was unspecified, even though these participants fulfilled the selection criteria for inclusion in the analysis.

smokers, with an average consumption of 10.3 (SD= 5.5) cigarettes/d. Further, 25.2% of the women drank alcohol, consuming an average of 1.2 (SD= 0.5) units/d. No other toxic habits were reported.

The percentages of women receiving pharmacological treatment for the presence of a vasomotor or genital syndrome (moderate to severe) are displayed in Figure 1A and B, respectively. Women with moderate-to-severe vasomotor syndrome were between 2.3 and 3 times more likely to be undergoing pharmacological treatment (any treatment for menopause, either nonspecific or specific to climacteric symptomatology, including MHT) compared with those without moderate or severe syndrome. In the case of genital syndrome, this significantly higher likelihood was only observed for the set of all treatments (any treatment) and for specific treatments (Fig. 1B). Table 2 and Figure 2 show the results of the ROC curve analysis for the various diagnostic test indicators, to test the criterion validity in the case of vasomotor syndrome. The cut-off point, for both the total score of the scale and its dimensions (which optimizes the indicators of sensitivity and specificity according to Youden's J index), is 25 points or more for moderate or severe vasomotor syndrome, particularly for vasomotor and menopausal dimensions and health, with area under the curve values $> 0.8$, diagnostic indicators close to or above 80% and diagnostic odds $> 10$. These results indicate that there is a greater likelihood of finding a woman with a score $> 25$ when the vasomotor syndrome is moderate or severe than when it is absent or mild and, therefore the likelihood of being under pharmacological treatment for menopausal symptoms is at least double or triple than nonsymptomatic women. Supplemental Digital Content Table S2, http://links.lww.com/MENO/A766 includes the coordinates of the ROC curve analysis for the total score and the dimensions of the Cervantes-SF scale for moderate or severe vasomotor syndrome. The criterion validity of the Cervantes-SF scale for moderate-to-severe genital syndrome did not present a cut-off point that adequately optimizes the diagnostic indicators (Supplemental Digital Content Figure S2, http://links.lww.com/MENO/A766).

Table 3 shows the predictive validity of the Cervantes-SF total score for health outcomes related to the degree of impairment in performing work and general daily activities, economic loss due to decreased work productivity, years of disability-free life expectancy, generic health status, hours of undisturbed sleep, and annual number of additional medical visits due to menopausal symptoms. This table also shows the magnitude of the MID in those outcomes in the event that the total score on the Cervantes-SF scale had a variation equal to or greater than a MID value of 6.7 points. Table 4 also shows the predictive validity of the Cervantes-SF total score for the above health outcome measures using the normative percentile values of the total score on the scale. This makes it possible to interpret the change that occurs in the health outcome when the total score of the scale changes from one percentile interval to another, either spontaneously or as the result of a health intervention.

## DISCUSSION

The Cervantes-SF scale has been shown to have good psychometric properties for measuring HRQoL in women with menopausal symptoms,[9] and, under conditions of routine medical practice it has been shown that women who choose menopausal hormone therapy for the treatment of menopausal symptoms have a poorer quality of life according to this scale.[30] However, until now, no tests have been conducted to confirm whether this instrument has the necessary properties for interpreting the health status of the population,[10,11] that is, criterion and predictive validity. Therefore—and as a complement to the validation of its main psychometric properties—the chief objective of this work was to confirm the


© 2021 The North American Menopause Society

Copyright © 2021 The North American Menopause Society. Unauthorized reproduction of this article is prohibited.

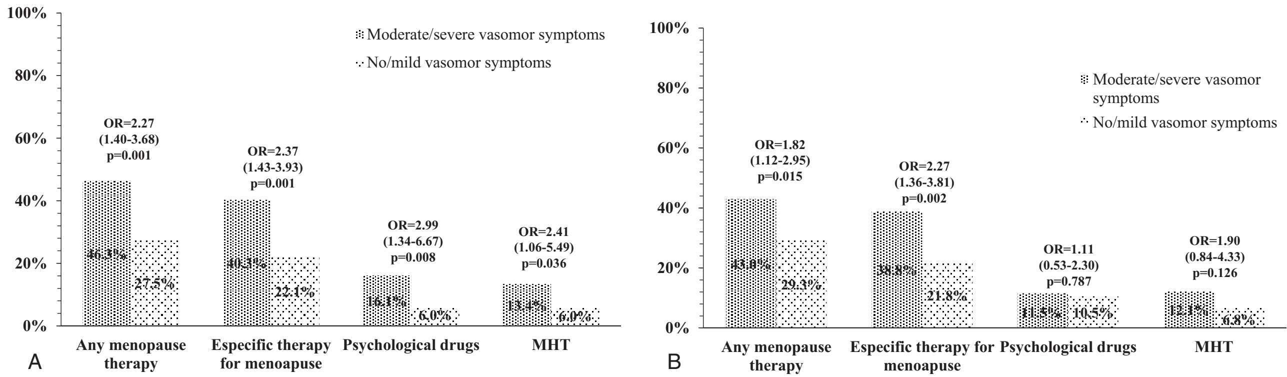


**FIG. 1.** Women receiving menopausal pharmacological therapy according to the presence of a moderate-to-severe menopausal vasomotor syndrome (**A**) or genital syndrome (**B**).

criterion and predictive validity of the Cervantes-SF scale. To test predictive validity, we used the variation of the scale score by a magnitude equal to or greater than 1 SEM, which is 6.7 points.[10] The SEM is considered a good indicator of the MID of any instrument and is interpreted as the difference that is perceived by the women when a change in their health has occurred that is detectable by themselves and, therefore, relevant.[26-29] That is, a variation (both increase and decrease) in the Cervantes-SF scale score of 6.7 or more points is due to a change in the woman's HRQoL in the peri/postmenopausal period that is perceived by the woman herself and indicates that she has experienced a change in her health status. Therefore, this could help to inform the decision making of the clinician responsible for the health care of the women.[26,30] The present study shows that a change of this magnitude predicts a minimally relevant change in the degree of impairment in work and general daily activities, economic impact due to decreased work productivity, disability-free life expectancy, generic health status, daily hours of undisturbed sleep, and annual medical visits related to menopausal symptoms. These data can facilitate interpretation of the scale score if used routinely in clinical practice. In fact, the predictive validity of the scale for the mentioned health outcomes was confirmed by using both the continuous total score of the scale and the percentiles, once each woman had been placed in relation to her reference population.

Moreover, we have confirmed the criterion validity of the scale for identifying women with moderate-to-severe vasomotor syndrome, but not for genital syndrome. The observed cut-off point, $>25$ points in the dimensions of menopause and health or in the subdimension of vasomotor problems (65% and 59% of the women in the sample obtained this score, respectively), has a sensitivity and specificity of approximately 80% or higher and a diagnostic odds ratio $>10$ for detecting a moderate-to-severe vasomotor syndrome. In our work, women with moderate-to-severe vasomotor syndrome were shown to have a two to three times greater likelihood of undergoing pharmacological treatment (mainly MHT) than women for whom the severity of the syndrome is absent or mild, which supports the ability of the scale to identify women who require MHT when they present menopause symptoms associated with a poor quality of life, as previously shown in routine clinical practice.[30] While the other dimensions or subdomains of the scale were unable to predict moderate-to-severe vasomotor syndrome, the predictive capacity of vasomotor and menopause and health subdomains for

**TABLE 2.** *Criterion validity of the abridged Cervantes-SF scale for the presence of moderate or severe vasomotor syndrome with a cutoff $>25$ points on the total score and dimensions*

| Dimension | Area under the curve (AUC) | Standard error | *P* | Sensitivity | Specificity | PPV | NPV | Youden,s J statistic | Diagnostic odds ratio | LR (+) | LR (−) |
|---|---|---|---|---|---|---|---|---|---|---|---|
| Total score | 0.798 | 0.026 | <0.001 | 79.2% | 63.8% | 68.6% | 75.4% | 0.415 | 6.7 (4.0-11.2) | 2.19 (1.74-2.75) | 0.33 (0.23-0.46) |
| Menopause and health | 0.883 | 0.020 | <0.001 | 81.9% | 77.9% | 78.7% | 81.1% | 0.588 | 15.9 (9.0-28.1) | 3.70 (2.71-5.04) | 0.23 (0.16-0.33) |
| Vasomotor | 0.923 | 0.017 | <0.001 | 89.9% | 81.9% | 83.2% | 89.1% | 0.711 | 40.4 (20.5-79.5) | 4.96 (3.51-7.01) | 0.12 (0.08-0.20) |
| Health | 0.720 | 0.030 | <0.001 | 58.4% | 71.8% | 67.4% | 63.3% | 0.307 | 3.6 (2.2-5.8) | 2.07 (1.55-2.77) | 0.58 (0.47-0.72) |
| Aging | 0.693 | 0.032 | <0.001 | 61.1% | 67.1% | 65.0% | 63.3% | 0.286 | 3.2 (2.0-5.2) | 1.86 (1.43-2.42) | 0.58 (0.46-0.73) |
| Sexuality | 0.567 | 0.035 | 0.053 | 75.5% | 37.5% | 55.2% | 60.0% | 0.125 | 1.9 (1.1-3.1) | 1.21 (1.03-1.41) | 0.65 (0.47-0.91) |
| Partner relationship | 0.556 | 0.035 | 0.108 | 39.6% | 67.4% | 55.0% | 52.5% | 0.077 | 1.4 (0.8-2.2) | 1.21 (0.88-1.66) | 0.90 (0.74-1.09) |
| Psychological | 0.698 | 0.031 | <0.001 | 51.7% | 71.1% | 64.2% | 59.6% | 0.249 | 2.6 (1.6-4.3) | 1.79 (1.33-2.41) | 0.68 (0.56-0.83) |

LR(−), likelihood ratio of a negative test (indicates how likely it is to find a score lower than the proposed cut-off point for criterion validity in women with moderate/severe vasomotor or genital syndrome compared with those without); LR(+), likelihood ratio of a positive test (indicates how likely it is to find a score higher than the proposed cut-off point for criterion validity in women with a moderate/severe vasomotor or genital syndrome compared with those without); NPV, negative predictive value; PPV, positive predictive value.



Copyright © 2021 The North American Menopause Society. Unauthorized reproduction of this article is prohibited.

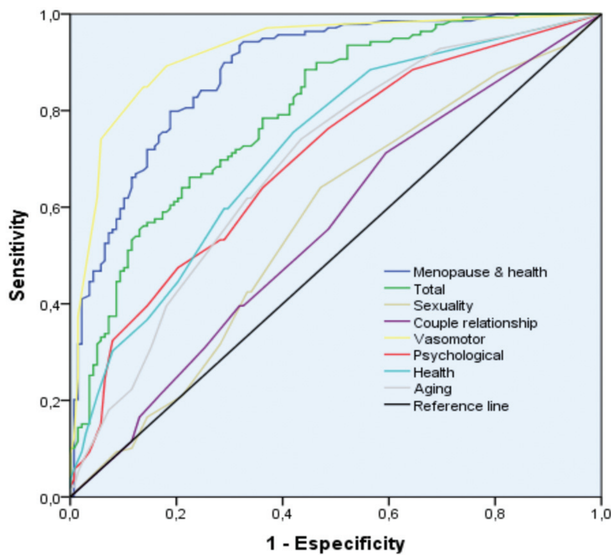


**FIG. 2.** Criterion validity of the Abbreviated Scale Cervantes-SF (total score and dimensions) for the presence of moderate-to-severe menopausal vasomotor syndrome.

vasomotor syndrome requiring treatment should not be a surprise since such domains are more directly related to vasomotor symptomatology. Thus, to illustrate, a hypothetical woman aged 55 years, active at work and in her menopause, who obtains a total score of 60 points on the Cervantes-SF scale, and 30 points on the vasomotor dimension, would have a more than 83% likelihood of having a moderate or severe vasomotor syndrome that requires pharmacological treatment, which is two and three times more likely than the case in which the vasomotor syndrome was absent or mild, respectively. Given that this woman is placed above the 90th percentile of the total score relative to her reference population according to the Cervantes-SF scale population norms, if a health intervention were not prescribed to improve her relative position, and her HRQoL was maintained at that score, this would have a negative impact on various health outcomes. This impact translates to a 20% work impairment with a resulting economic loss that is equivalent to 6,066 euros per year, a 42% impairment in carrying out general daily activities, a 31% deterioration in general health status, a loss of 9.7 years of disability-free life expectancy, a loss of 4.7 hours of undisturbed sleep per day and a 0.5 increase in the annual number of visits to family medical or gynecology clinics.

**TABLE 3.** *Predictive validity of the total score of the Cervantes-SF abbreviated scale according to different health outcomes*

| Health outcomes | β Coefficient [a] (standard error) | 95% CI of the β coefficient | *P* | $R^2$ adjusted | Durbin-Watson | Collinearity statistics: Tolerance | Collinearity statistics: VIF | Minimally relevant change (95% CI)[b] |
|---|---|---|---|---|---|---|---|---|
| Impairment in work activity, % (WPAI-GH) | 0.295 (0.078) | 0.141-0.449 | <0.001 | 0.106 | 2.05 | 0.965 | 1.036 | ±2.0% (1.0%-3.0%) |
| Economic loss per person per year due—decreased work productivity (€, year 2018)[c] | 91.0 (24.1) | 43.5-138.5 | <0.001 | 0.106 | 2.05 | 0.965 | 1.036 | ±610€ (292€-928€) |
| General impairments in carrying out daily living activities, % (WPAI-GH) | 0.619 (0.075) | 0.470-0.767 | <0.001 | 0.230 | 1.54 | 0.969 | 1.032 | ±4.2% (3.2%-5.1%) |
| Generic quality of life, VAS points EQ-5D-3L (range: 0-100) | −0.457 (0.058) | −0.571 to −0.334 | <0.001 | 0.215 | 1.87 | 0.979 | 1.022 | ±3.1% (2.2%-3.8%) |
| Years of healthy life expectancy without disability (DALE)[d], years | −0.125 (0.023) | −0.171 to −0.079 | <0.001 | 0.376 | 1.85 | 0.902 | 1.108 | ±0.8 (0.5-1.1) y |
| Effective daily sleep hours (without interruption)[e] | −0.069 (0.008) | −0.085 to −0.052 | <0.001 | 0.258 | 1.89 | 0.917 | 1.090 | ±0.5 (0.4-0.6) h |
| Variation in annual medical visits due to menopausal symptoms | 0.008 (0.002) | 0.004-0.012 | <0.001 | 0.103 | 1.99 | 0.948 | 1.055 | ±0.6 (0.3-1.0) visits |

INE, Instituto Nacional de Estadística; VAS, visual analog scale or health thermometer as a percentage, measured by the EQ-5D-3L questionnaire, ranging from 0 [worst imaginable health] to 100 [perfect health]; VIF, variance inflation factor; WPAI-GH, work productivity and activity impairment questionnaire-general health, ranging from 0% [no loss of work productivity/daily life activities] to 100% [complete loss of work productivity/daily life activities].
[a]β Coefficient estimated for the total score of the scale in continuous range 0 to 100 by means of multiple linear regression models using stepwise elimination with the following covariates: age (years), body mass index (kg/$m^2$), education level, marital status, menopausal status (peri- or postmenopausal), age at menarche (years), number of comorbidities and their severity according to Charlson's eight-item abbreviated severity index (0-10 points), tobacco consumption (yes/no), alcohol consumption (yes/no), and pharmacological treatment of climacteric syndrome (yes/no).
[b]Minimally relevant change is obtained by multiplying the β-coefficient of each outcome by the value of the minimally important difference (MID) of the total score of Cervantes-SF scale and is expected to occur when the change in health-related quality of life of a menopausal woman due to menopausal symptoms is of a magnitude above or below one time the MID. In the total score of the Cervantes-SF scale, the magnitude of the MID is equivalent to one time the standard error of measurement (SEM), which is of a magnitude equal to 6.7 points in the total score of the scale (see Reference 7).
[c]Calculated as the product of the % of impairment/loss of work activity due to menopausal symptoms multiplied by the average labor cost for 2018 in Spain according to the INE labor cost survey (30.883,44 €, Source: INE, 2018).
[d]DALE, disability-adjusted life-expectancy or years of healthy life expectancy without disability (see the Methods section for an explanation of its calculation).
[e]Hours of undisturbed daily sleep (see the Methods section for an explanation of its calculation).


*© 2021 The North American Menopause Society*

Copyright © 2021 The North American Menopause Society. Unauthorized reproduction of this article is prohibited.

**TABLE 4.** *Predictive validity of the total score of the Cervantes-SF scale for different health outcomes expressed as the normative percentile values of the scale*

| Health outcomes | β Coefficient [a] (standard error) | 95% CI of the β coefficient | *P* | $R^2$ adjusted | Durbin-Watson | Collinearity statistics: Tolerance | Collinearity statistics: VIF |
|---|---|---|---|---|---|---|---|
| Impairments in work activity, % (WPAI-GH) | 3.28 (0.99) | 1.33-5.22 | 0.001 | 0.096 | 1.97 | 0.955 | 1.048 |
| Economic loss per person per year due to decreased work productivity (€, year 2018)[b] | 1.011 (304) | 411-1,612 | 0.001 | 0.096 | 1.97 | 0.955 | 1.048 |
| Overall impairment in carrying out daily living activities, % (WPAI-GH) | 7.00 (0.94) | 5.14-8.86 | <0.001 | 0.208 | 2.08 | 0.973 | 1.028 |
| Generic Quality of Life, VAS points EQ-5D-3L (range: 0-100) | −5.14 (0.66) | −6.45 to −3.83 | <0.001 | 0.233 | 2.16 | 0.977 | 1.024 |
| Years of healthy life expectancy without disability (DALE)[c], years | −1.62 (0.23) | −2.08 to −1.17 | <0.001 | 0.539 | 1.71 | 0.926 | 1.080 |
| Effective daily sleep hours (without interruption)[d] | −0.78 (0.10) | −0.97 to −0.59 | <0.001 | 0.252 | 0.93 | 0.931 | 1.074 |
| Variation in annual medical visits due to menopausal symptoms | 0.09 (0.02) | 0.05-0.14 | <0.001 | 0.106 | 1.98 | 0.971 | 1.030 |

INE, Instituto Nacional de Estadística; VAS, visual analog scale or health thermometer as a percentage, measured by the EQ-5D-3L questionnaire, ranging from 0 [worst imaginable health] to 100 [perfect health]; VIF, variance inflation factor; WPAI-GH, work productivity and activity impairment questionnaire-general health, range 0% [no loss of work productivity/daily life activities] to 100% [complete loss of work productivity/daily life activities].
[a]β Coefficient estimated for the total score of the scale clustered into normative percentiles (<P10=1; P10-<P25=2; P25-<P50=3; P50-<P75=4; P75-<P90=5 and ≥P90=6) by means of multiple linear regression models using stepwise elimination with the following covariates: age (years), body mass index (kg/m²), education level, marital status, menopausal status (peri- or postmenopausal), age at menarche (years), number of comorbidities and their severity according to Charlson's eight-item abbreviated severity index (0-10 points), tobacco consumption (yes/no), alcohol consumption (yes/no), and pharmacological treatment for climacteric syndrome (yes/no).
[b]Calculated as the product of the % impairment/loss of work activity due to menopausal symptoms multiplied by the average labor cost for 2018 in Spain according to the INE labor cost survey (30,883.44 € Source: INE, 2018).
[c]DALE, disability-adjusted-life-expectancy or years of healthy life expectancy without disability (see the Methods section for explanation of its calculation).
[d]Hours of daily sleep without interruption (see the Methods section for an explanation of its calculation).

A number of other scales and instruments have been used to measure the impact of peri/postmenopausal symptoms on women's HRQoL.[31] These include the questionnaire, originally developed in Spanish, known as the Menopause and Quality of Life Scale [32] along with other menopause-related questionnaires that have been developed internationally, such as the Menopause Specific Quality of Life Questionnaire,[33] the Greene Climacteric Scale,[34] the Woman's Health Questionnaire,[35] or the Menopause Rating Scale.[36] And whilst some of these instruments have been adapted to Spanish, none have shown the properties of criterion or predictive validity evaluated in our research. Therefore, we believe that, in terms of utility and interpretability, the findings of the present study provide further support for the value of using the Cervantes-SF scale in preference to other existing instruments.

This work is not exempt from limitations. Our sample was recruited from a real-world context of daily clinical practice and although this is representative from a clinical point of view, we cannot rule out the possibility that selection bias could have produced an imbalance in the composition of the sample in terms of age, socioeconomic level, and education. Thus, in future studies it will be necessary to confirm the present findings in a sample of menopausal women that is more representative in terms of age, socioeconomic, educational, and cultural variables. Finally, although the scale has criterion validity for moderate-to-severe vasomotor syndrome, it has not been possible to confirm this attribute for genital syndrome.

## CONCLUSION

Despite these potential limitations, the results presented here confirm, for the Cervantes-SF scale, both the predictive validity of the scale for health outcomes related to various aspects of women's daily life during menopause, and criterion validity for identifying women with moderate-to-severe vasomotor syndrome requiring pharmacological treatment.

**Acknowledgments:** The authors thank the Spanish Menopause Society for its support and guidance.

The AEEM group responsible for the development of the Cervantes-SF scale is composed of: Pluvio J. Coronado (Hospital Clínico San Carlos, Madrid), Rafael Sánchez-Borrego (Clínica DIATROS, Barcelona), Laura Baquedano (Hospital Universitario Miguel Servet, Zaragoza), Sonia Sánchez (Hospital Sagrado Corazón, Barcelona), Cristina Argudo (Clínica Begoña, Gijón, Asturias), Micaela Fernández-Abellán (Clínica Quirón, Málaga), Silvia González (Gabinete Médico Velázquez, Madrid), Eva Iglesias (Hospital de Valme, Sevilla), Jackie Calleja (Clínica Quirón, Madrid), Jesús Presa (Hospital Clínico de Jaén), Alfonso Duque (Clínica Ruber, Madrid), Fernando Ruiz (Hospital Clínico Universitario, Valencia), Borja Otero (Hospital Universitario de Cruces, Baracaldo, Vizcaya), María Fasero (Hospital Sanitas La Zarzuela, Madrid), Plácido Llaneza (Hospital Universitario Central de Asturias, Gijón, Asturias)



Copyright © 2021 The North American Menopause Society. Unauthorized reproduction of this article is prohibited.

and Santiago Palacios (Instituto Palacios de Salud y Medicina de la Mujer, Madrid).

## REFERENCES

1. Mendoza N, Juliá MD, Galliano D, et al. Spanish consensus on premature menopause. *Maturitas* 2015;80:220-225.
2. Vélez Toral M, Godoy-Izquierdo D, Padial García A, et al. Psychosocial interventions in perimenopausal and postmenopausal women: a systematic review of randomised and non-randomised trials and non-controlled studies. *Maturitas* 2014;77:93-110.
3. Avis NE, Stellato R, Crawford S, et al. Is there a menopausal syndrome? Menopausal status and symptoms across racial/ethnic groups. *Soc Science Med* 2001;52:345-356.
4. Meeuwsen IB, Samson MM, Duursma SA, Verhaar HJ. The influence of tibolone on quality of life in postmenopausal women. *Maturitas* 2002;41:35-43.
5. Mendoza N, Abad P, Baró F, et al. Spanish Menopause Society position statement: use of tibolone in postmenopausal women. *Menopause* 2013;20:754-760.
6. Palacios S, Ferrer-Barriendos J, Parrilla JJ, et al. Calidad de vida relacionada con la salud en la mujer española durante la perimenopausia y posmenopausia. Desarrollo y validación de la Escala Cervantes. *Med Clin (Barc)* 2004;122:205-211.
7. Coronado P, Sánchez Borrego R, Palacios S, Ruiz MA, Rejas J. Structural validity of a 16-item abridged version of the Cervantes health-related quality of life scale for menopause: the Cervantes Short-Form scale. *Menopause* 2015;22:325-336.
8. Coronado PJ, Sánchez-Borrego R, Ruiz MA, et al. Psychometric attributes of the Cervantes short-form questionnaire for measuring health-related quality of life in menopausal women. *Maturitas* 2016;84:55-62.
9. Aaronson N, Alonso J, Burnam A, et al. Assessing health status and quality-of-life instruments: attributes and review criteria. *Qual Life Res* 2002;11:193-205.
10. Chassany O, Sagnier P, Marquis P, Fullerton S; Aaronson N for the European Regulatory Issues on Quality of Life Assessment Group. Patient-reported outcomes: the example of health-related quality of life: a European guidance document for the improved integration of health-related quality of life assessment in the drug regulatory process. *Drug Inform J* 2002;36:209-238.
11. Nunnally JC, Bernstein IH. *Psychometric Theory.*, 3rd ed. New York: McGraw-Hill; 1994.
12. Fayers PM, Machin D. *Quality of Life: The Assessment, Analysis and Interpretation of Patient-Reported Outcomes*, 2nd ed. Chichester, UK: John Wiley and Sons, Ltd; 2007; 1-10.
13. STROBE Statement. Home. Available at: https://strobe-statement.org/index.php?id=strobe-home. Accessed June 2020.
14. Harlow SD, Gass M, Hall JE, et al; STRAW + 10 Collaborative Group. Executive summary of the Stages of Reproductive Aging Workshop + 10: addressing the unfinished agenda of staging reproductive aging. *J Clin Endocrinol Metab* 2012;97:843-851.
15. ACOG Practice Bulletin No. 141: management of menopausal symptoms. Obstet Gynecol. 2014; 123(1):202-16. PMID: 24463691 Available at: www.ncbi.nlm.nih.gov/pubmed/24463691. Accessed April 20, 2020.
16. 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;20:518-524.
17. Centers for Disease Control and Prevention (CDC) NHANES 2009-2010. National Center for Health Statistics (NCHS). Available at: http://wwwn.cdc.gov/nchs/nhanes/search/nhanes09_10.aspx. Accessed October 9, 2013.
18. EuroQol Group. EuroQol—a new facility for the measurement of health-related quality of life. *Health Policy* 1990;16:199-208.
19. Reilly MC, Zbrozek AS, Dukes EM. The validity and reproducibility of a work productivity and activity impairment instrument. *Pharmacoeconomics* 1993;4:353-365.
20. Kim MJ, Yim G, Park HY. Vasomotor and physical menopausal symptoms are associated with sleep quality. *PLoS One* 2018;13:e0192934.
21. Mathers CD, Sadana R, Salomon JA, Murray CJL, Lopez AD. Estimates of DALE for 191 countries: methods and results. Global Programme on Evidence for Health Policy Working Paper No. 16. *World Health Organization* 2000.
22. INE, 2018. Encuesta de costes laborales. Disponible en: Available at: https://www.ine.es/dyngs/INEbase/es/operacion.htm?c=Estadistica_C&cid=1254736060920&menu=ultiDatos&idp=1254735976596. Accessed April 20, 2020.
23. Mendoza N, Sánchez-Borrego R, Cancelo MJ, et al. Position of the Spanish Menopause Society regarding the management of perimenopause. *Maturitas* 2013;74:283-290.
24. Schisterman EF, Perkins NJ, Liu A, Bondell H. Optimal cut-point and its corresponding Youden Index to discriminate individuals using pooled blood samples. *Epidemiology* 2005;16:73-81.
25. Berkman LF, Leo-Summers L, Horwitz RI. Emotional support and survival after myocardial infarction. A prospective, population-based study of the elderly. *Ann Intern Med* 1992;117:1003-1009.
26. Guyat GH, Osoba D, Wu AW, Wyrwich KW, Norman GR; and the clinical significance consensus meeting group. Methods to explain the clinical significance of Health Status Measures. *Mayo Clinic Proc* 2002;77:371-383.
27. Revicki D, Hays RD, Cella D, Sloan J. Recommended methods for determining responsiveness and minimally important differences for patient-reported outcomes. *J Clin Epidemiol* 2008;61:102-109.
28. Rejas J, Pardo A, Ruiz MA. Standard error of measurement as a valid alternative to minimally important difference for evaluating the magnitude of changes in patient-reported outcomes measures. *J Clin Epidemiol* 2008;61:350-356.
29. Wyrwich KW, Tierney WM, Wolinsky FD. Further evidence supporting an SEM-based criterion for identifying meaningful intra-individual changes in health-related quality of life. *J Clin Epidemiol* 1999;52:861-873.
30. Fasero M, Hernández A, Varillas-Delgado D, Coronado PJ. Women with low quality of life by Cervantes-short form scale choose menopausal hormone therapy. *Eur J Obstet Gynecol Reprod Biol* 2020;252:43-49.
31. Jenabi1 E, Shobeiri1 F, Hazavehei SMM, Roshanaei G. Assessment of Questionnaire Measuring Quality of Life in Menopausal Women: a systematic review. *Oman Med J* 2015;30:151-156.
32. Buendía A, Bermejo J, Rodríguez Segarra R, Yubero Bascuñana N, Martínez Vizcaíno V. Diseño y validación de un cuestionario en castellano para medir la calidad de vida en mujeres posmenopáusicas: el cuestionario MENCAV. *Aten Primaria* 2001;27:94-100.
33. Hilditch JR, Lewis J, Peter A, et al. A menopause-specific quality of life questionnaire: development and psychometric properties. *Maturitas* 1996;24:161-175.
34. Greene JG. Constructing a standard climacteric scale. *Maturitas* 2008;29:25-31.
35. Hunter MS. The Women's Health Questionnaire (WHQ): frequently asked questions (FAQ). *Health Qual Life Outcomes* 2003;1:41.
36. Hauser GA, Huber IC, Keller PJ, Lauritzen C, Schneider HPG. *Evaluation der klinischen Beschwerden (Menopause Rating Scale) Zentralbl Gynakol* 1994;116:16-23.

 © 2021 The North American Menopause Society

Copyright © 2021 The North American Menopause Society. Unauthorized reproduction of this article is prohibited.