Maturitas 111 (2018) 15–19

Contents lists available at ScienceDirect

Maturitas

journal homepage: www.elsevier.com/locate/maturitas

Decision-making for the treatment of climacteric symptoms using the Menopause Rating Scale

Juan Enrique Blümel[a,*], Eugenio Arteaga[b], Joaquín Parra[a], Carolina Monsalve[a], Valentina Reyes[a], María Soledad Vallejo[c], Rosa Chea[a]

[a] Department of Internal Medicine (South), Faculty of Medicine, Universidad de Chile, Santiago, Chile
[b] Department of Endocrinology, Faculty of Medicine, Pontificia Universidad Católica de Chile, Santiago, Chile
[c] Ginecología Obstetricia, Clínica Quilín, Universidad de Chile, Chile

ARTICLE INFO

Keywords:
Menopause Rating Scale
Climacteric symptoms
Menopause therapy
Patient decision-making

ABSTRACT

Objective: The Menopause Rating Scale (MRS) is one of the most frequently used instruments to evaluate menopausal symptoms; however, no cut-off score is given that would indicate the need for treatment. Our goal was to determine such a cut-off score on the MRS, using as a standard a woman's own perception of her need for treatment in relation to the severity of her symptoms.

Material and methods: The sample comprised 427 healthy women aged 40–59 years who were not taking hormonal treatment. Based on the concept of quality of life, we considered that the patient required treatment if she herself believed that she required it, on the basis of the severity of at least one of her menopausal symptoms. To obtain an optimal MRS cut-off score associated with the need for treatment, an ROC curve analysis was performed.

Results: The symptoms rated "very severe" on the MRS (i.e. that most require treatment) were physical and mental exhaustion (95.8% of women) and muscle and joint discomfort (95.1%). In total, 378 women (88.5%) considered that their symptoms required treatment. The ROC curve analysis determined that the optimal cut-off score on the MRS to indicate the need for treatment would be 14 (area under the curve 0.86, $p < 0.0001$). This score achieved 76.5% sensitivity and 83.6% specificity. With this cut-off score, 97.1% of the women who considered that they required treatment for at least one of their symptoms would be treated. There was concordance of more than 90% between this cut-off score and a score of 4 (i.e. a rating of "very severe") for any of the symptoms on the scale.

Conclusions: An MRS score ≥14 indicates the need for treatment for climacteric symptoms. In clinical practice, a score of 4 for any of the MRS items could be taken to indicate the need for treatment.

1. Introduction

The 2017 Position Statement of the North American Menopause Society (NAMS) considers that menopausal hormonal therapy (MHT) is "the most effective treatment for vasomotor symptoms (VMS) and the genito-urinary syndrome (GSM) of menopause" [1]. The intensity of climacteric symptoms varies in different women, from light disturbances not requiring treatment to severe symptoms which greatly reduce quality of life. The Position Statement of the NAMS does not state when it is desirable to initiate MHT; while it does say that "bothersome VMS" can be taken to indicate the need for treatment, it does not go on to define "bothersome".

The "Revised Global Consensus Statement on Menopausal Hormone Therapy" produced by the International Menopause Society states that "the option of MHT is an individual decision in terms of quality of life and health priorities as well as personal risk factors such as age, time since menopause and the risk of VTE, stroke, ischemic heart disease and breast cancer. MHT should not be recommended without a clear indication for its use" [2]. However, it does not define the meaning of "a clear indication for its use".

The US Food and Drug Administration (FDA) defines health-related quality of life as "the patients' evaluation of the impact of a health condition and its treatment on daily life" [3]. Similarly, the UK National Institute for Health and Care Excellence (NICE), in a Clinical Guideline, defines a complaint as severe when it 'interferes with a womańs physical, emotional, social and material quality of life' [4]. Thus,

* Corresponding author at: Departamento Medicina Sur, Facultad de Medicina, Universidad de Chile, Orquídeas 1068, Dpto 302, PO Box 7510258, Providencia, Santiago de Chile, Chile.
E-mail address: juan.blumel@redsalud.gov.cl (J.E. Blümel).

https://doi.org/10.1016/j.maturitas.2018.02.010
Received 14 November 2017; Received in revised form 5 February 2018; Accepted 13 February 2018

considering the concept of quality of life, the decision to prescribe MHT should take account of the perception of the patient regarding the severity of her climacteric symptoms. That is, it is the patient who should decide whether treatment is needed.

Different instruments have been designed for the recognition and measurement of the impact of climacteric symptoms on quality of life. The Menopause Rating Scale (MRS) is an instrument with known psychometric properties, that has been validated in several languages and that is the most extensively used around the world to evaluate the severity of symptoms associated with menopause [5]. However, although this instrument is used worldwide, some caution is warranted in interpreting scores, since the prevalence of climacteric symptoms can differ across countries because of genetic, sociocultural and lifestyle factors [6]. While a total score of 17 or more on the MRS is stated to indicate "severe symptomatology", no cut-off score is given that could be taken as an objective indication of the need for treatment. It would be ideal to determine such a cut-off score for this instrument.

The goal of our study was to find a cut-off score on the Menopause Rating Scale which would allow us to make a better decision regarding the need to start treatment, using as a standard the woman's own perception of the severity of her symptoms.

2. Subjects and methods

2.1. Participants

A group of 500 women aged 40–59 years, with self-reported normal health, defined as their capacity to perform all their routine activities [7], were asked to complete the MRS. All the participants were companions of patients attending the Diagnostic Center, Hospital Barros Luco, Santiago de Chile.

We used the statistics program Epi Info 7.2 to calculate the sample size, with an expected frequency of severe climacteric symptoms of 40% [8], with a total population of 150,000 women aged 40–59 years [9] and an acceptable maximum error of 5% and with 95% confidence. With these parameters we concluded that the minimum sample size was 369 women. Five hundred women were surveyed, in case it was necessary to eliminate some cases due to incomplete data and also to perform subgroup analyses. The principal inclusion criterion was adequate health to perform routine activities and the principal exclusion criteria were mental deficiency that prevented a woman from understanding the questionnaire, and the use of oral contraceptives or MHT.

2.2. Instrument

The validated Spanish version of the MRS was used [10]. It is a questionnaire composed of 11 items (symptoms), divided into three domains:

- Somatic – hot flushes, excessive perspiration; heart discomfort; sleep problems; muscle and joint discomfort (items 1–3 and 11, respectively)
- Psychological – depressive mood; irritability; anxiety; physical and mental exhaustion (items 4–7, respectively)
- Urogenital – sexual problems; bladder problems; vaginal dryness (items 8–10, respectively).

For each item, the women assigns a score of 0–4 for the intensity of the symptom (0, absent; 1, mild; 2, moderate; 3, severe; 4, very severe). The score on a particular domain corresponds to the sum of the values obtained for each item of the subscale. The total MRS score is the sum of the scores obtained in each domain. Based on the concept of quality of life, which includes the woman's perception of the severity of the symptomatology, to evaluate the need to prescribe MHT, we additionally asked with every MRS question: "Do you believe that the severity of this particular symptom requires treatment?" We considered that the patient required treatment if she answered yes in relation to any of the 11 items of the MRS.

2.3. Statistical analysis

Data analysis was performed using the IMB SPSS 21 statistical package. Results are presented as means ± standard deviations, percentages and odds ratios (with 95% confidence intervals, CI). To obtain the optimal MRS cut-off score to indicate the need for treatment, receiver operator characteristic (ROC) curve analysis was performed (SPSS 21). The optimal cut-off score was determined by plotting for each score the true-positive rate (sensitivity) against the false-positive rate (1-specificity), and ascertaining when the maximum accuracy (sensitivity plus specificity) was achieved. In addition, cut-off values were assessed based on the maximum values of the Youden Index (calculated as sensitivity + specificity-1) and the minimum values of the square root of [(1 − sensitivity)2 + (1 − specificity)2], which indicates the minimum distance from the upper-left corner to the value on the ROC curve [11,12].

2.4. Ethics

This study was approved by the Comité de Ética del Servicio de Salud Metropolitano Sur, Santiago, Chile, according to the Helsinki Declaration [13]. All participants gave informed consent for the use of their data to perform clinical studies, maintaining confidentiality.

3. Results

Of the 518 women invited to participate in this study, 500 (96.5%) agreed to do so. We eliminated a further 48 women because they used oral contraceptives and 25 because they used MHT. As shown in Table 1, the mean age of the remaining sample of 427 women was 50.5 ± 5.4 years; most of them had a low level of education; 84.3% attended public health services; 68.9% had a stable partner; 63.7% were postmenopausal; 17.6% used psychotropic drugs; and 18.7% had a previous psychiatric consultation.

In Table 2 shows the ratings for the different climacteric symptoms included on the MRS. The symptoms most commonly rated "very severe" (i.e. a score of 4 on the MRS) were muscle and joint discomfort (42.9% of all women), followed by physical and mental exhaustion (33.7%), depressive mood (33.3%) and sleep problems (31.1%).

Table 1
Characteristics of the women in the study (n: 427).

Variable	Means ± SD or Number of women (percentage; IC 95%)
Age (years)	50.5 ± 5.4
Total time in education (years)	11.0 ± 3.3
Attending public health services	360 (84.3; 80.8–87.6)
With a stable partner (%)	294 (68.9; 64.6–73.1)
With sexual activity (%)	296 (69.3; 64.9–73.5)
Premenopausal (%)	60 (14.1; 10.8–17.3)
Perimenopausal (%)	95 (22.2; 18.5–26.5)
Postmenopausal (%)	272 (63.7; 59.3–68.1)
Hysterectomy (%)	63 (14.8; 11.5–18.3)
Bilateral oophorectomy (%)	22 (5.2; 3.0–7.3)
Use of psychotropic drugs (%)	75 (17.6; 14.3–21.1)
Previous psychiatric consultation (%)	80 (18.7; 15.2–22.5)

Table 2
Percentage of women giving different ratings of the severity of their climacteric symptoms on the MRS.

Symptom (MRS)	Intensity of symptom (score)				
	Absent (0)	Mild (1)	Moderate (2)	Severe (3)	Very severe (4)
Hot flushes, sweating	25.8	15.0	16.6	13.8	28.8
Heart discomfort	34.9	16.9	18.7	13.8	15.7
Sleep problems	29.7	10.5	13.8	14.8	31.1
Muscle and joint discomfort	13.1	11.0	17.3	15.7	42.9
Depressive mood	22.5	13.8	17.1	13.3	33.3
Irritability	23.4	17.8	19.4	14.5	24.8
Anxiety	36.3	12.9	14.8	10.8	25.3
Physical and mental exhaustion	16.2	15.0	18.3	16.9	33.7
Sexual problems	36.8	11.9	14.8	11.9	24.6
Bladder problems	58.1	11.9	8.4	8.2	13.3
Vaginal dryness	55.5	15.2	8.9	8.2	12.2

Vaginal dryness (12.2%), bladder problems (13.3%) and heart discomfort (15.7%) were infrequently rated very severe.

In Table 3 shows the percentages of women who considered that they required treatment, grouped according to the intensity of each of the symptoms on the MRS. As the severity rating of a symptom increases, the percentage of women who feel they require treatment also increases, reaching a level of 90% in those who consider that at least one of their symptoms is very severe. The symptoms that most commonly deemed to require treatment when rated "very severe" were: physical mental exhaustion (95.8%), muscle and joint discomfort (95.1%) and bladder problems (94.2%). Those symptoms that least frequently considered to require treatment were: sexual problems (79.0%), anxiety (86.1%) and heart discomfort (86.6%). In total, 378 women (88.5%) considered that they required some type of therapy because of the severity of their symptomatology.

ROC curve analysis was used to obtain an optimal MRS cut-off score capable of objectively defining the need for treatment, using as a reference the perception of the women regarding the need for treatment, independently of the severity of the symptoms. The area under the ROC curve was 0.86 (95% CI, 0.81–0.91) (Fig. 1). Differences between the areas under the ROC curve were significant ($p < 0.0001$). For women

Table 3
Percentages of women who considered that they required treatment for their climacteric symptoms, by MRS scores for individual items.

Symptoms (MRS)	MRS score				
	Absent (0)	Mild (1)	Moderate (2)	Severe (3)	Very severe (4)
Hot flushes, sweating	5.5	53.1	59.2	79.7	90.2
Heart discomfort	6.0	44.4	66.3	78.0	86.6
Sleep problems	6.3	31.1	61.0	79.4	90.2
Muscle and joint discomfort	8.9	42.6	64.9	86.6	95.1
Depressive mood	4.2	39.0	54.8	73.7	91.5
Irritability	0.0	25.0	49.4	74.2	87.7
Anxiety	4.5	45.5	57.1	80.4	86.1
Physical and mental exhaustion	4.3	45.3	67.9	80.6	95.8
Sexual problems	3.2	17.6	54.0	66.7	79.0
Bladder problems	4.6	43.1	68.4	91.4	94.2
Vaginal dryness	5.6	43.1	61.1	97.1	87.7

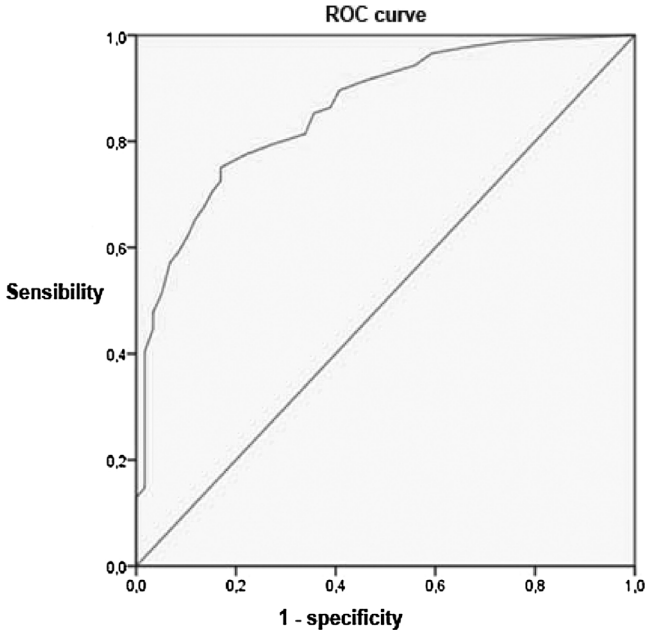

Fig. 1. ROC curve analysis used to obtain an optimal MRS score cutoff value to treat menopausal symptoms.

with an MRS score of 14 or more, the minimum distance to ROC curve was 0.081, and the maximum Youden Index value was 0.601. This cut-off score of 14 points on the MRS had 76.5% sensitivity and 83.6% specificity. Of the women who considered that they required treatment for at least one of their symptoms, 97.1% would be treated on the basis of an MRS cut-off score of 14 points.

Table 4 shows that if we had used a cut-off score of 14 points on the MRS to determine the need for therapy, the concordance for any of the symptoms evaluated with the MRS among women who think they require some therapy for their symptomatology and that cut-off score ranges from 81.3% to 91.6%. The highest level of agreement was found for depressive mood (91.6%), followed by irritability (91.0%) and anxiety (90.4%). The lowest level of agreement was muscle and joint discomfort (81.3%), bladder problems (84.2%) and physical and mental exhaustion (85.4%).

If we evaluate the concordance between a rating of "very severe" (a score of 4) for any of the MRS climacteric symptoms and a total MRS score of 14 or more we can see that this figure fluctuates between 92.3% and 100% (Table 5). The highest concordance (100%) is for heart discomfort, followed by sexual problems (99.0%) and physical

Table 4
Concordance among women who perceive they require treatment due to the severity of their climacteric symptoms and a score of 14 in the MRS as a cut-off point to indicate the need for therapy (n: 427 women).

Symptom	N° of women who perceive they require treatment	N° of women (%) scoring ≥14 on the MRS
Hot flushes, sweating	240	209 (87.1)
Heart discomfort	198	175 (88.4)
Sleep problems	228	205 (89.9)
Muscle and joint discomfort	305	248 (81.3)
Depressive mood	239	219 (91.6)
Irritability	199	181 (91.0)
Anxiety	198	179 (90.4)
Physical and mental exhaustion	281	240 (85.4)
Sexual problems	165	147 (89.1)
Bladder problems	146	123 (84.2)
Vaginal dryness	142	126 (88.7)

Table 5
Agreement between women who present "very severe" climacteric symptoms (a score of 4 on the MRS) and 14 points as the cut-off score for the initiation of therapy.

Symptom	N° of women who have a score of 4 for any symptom (total of 427 women)	N° of women (%) with a total MRS score ≥14
Hot flushes, sweating	123	116 (94.3)
Heart discomfort	67	67 (100.0)
Sleep problems	133	129 (97.0)
Muscle and joint discomfort	183	175 (95.6)
Depressive mood	142	137 (96.5)
Irritability	106	104 (98.1)
Anxiety	108	105 (97.2)
Physical and mental exhaustion	144	142 (98.6)
Sexual problems	105	104 (99.0)
Bladder problems	52	48 (92.3)
Vaginal dryness	57	55 (96.5)

and mental exhaustion (98.6%). The lowest concordance is for bladder problems (92.3%), hot flushes and sweating (94.3%) and muscle and joint discomfort (96.5%).

4. Discussion

This study shows that a large proportion of women, between 15% and 42%, rate the individual climacteric symptoms on the MRS "very severe". Our data agree with the mean of 25% of symptoms being rated "severe" published by the original authors of the MRS for developed occidental countries [14]. In this study, the classic vasomotor symptoms were not the complaints that were of most concern. We have previously found, in 8373 women aged 40–59 years from 12 Latin-American countries that vasomotor symptoms were in the ninth place in prevalence among the 11 symptoms evaluated by the MRS [15].

The study highlights the high percentage of women who consider that their symptoms are severe enough to require some type of treatment. As expected, this percentage increases with the severity of the climacteric symptomatology, reaching around 90% of women who rate one of the symptoms evaluated by MRS "very severe". Women's opinion is essential in the decision to initiate therapy, as reflected in the importance attached to the concept of "shared decision-making" between the physician and the patient [16]. NICE guidelines, referring to MHT, state: "Offer women HRT for vasomotor symptoms after discussing with them the short-term (up to 5 years) and longer-term benefits and risks". This phrase clearly implies that every woman, after being informed by the physician, must decide whether or not to receive MHT [17].

A cut-off score of 14 points on the MRS detected around 90% of those women who perceived that they required treatment for any one of the individual MRS symptoms; this discriminating capacity was similar for all 11 MRS items.

The MRS authors gave a cut-off score 17 as a threshold to define overall climacteric symptomatology as very severe [14], but not necessarily to treat it, which implies that total scores below 17 could require treatment, as indeed was found in our study. This is not surprising, since a woman could have a total score below 17 while still having one or two symptoms rated very severe, with a score of 4.

We have not found in the medical literature a study evaluating a cut-off score on the MRS to initiate therapy. We have found only a poster on the MRS website which was presented in the 2005 Congress of the International Society of Pharmacoepidemiology (Nashville, USA). It reports an evaluation of the efficacy of the MRS score to determine whether a treatment had a good therapeutic response; the conclusion was that an MRS score improvement of at least 4–7 points is recommended to establish clinical meaningful efficacy [18]. Another study sought to find an MRS cut-off score for a patient referral to a gynecologist, and determined that with 16 points there was a high probability that a patient would be referred to a specialist [19].

The cut-off score of 14 that we have described in the present study as a threshold for the prescription of therapy for climacteric symptoms objectively quantifies a clinical behavior and could be useful for research studies, but in clinical practice the presence of a single symptom rated with a score 4 on the MRS would be sufficient. In the present study, we observed that there is concordance of more than 90% between a total MRS score of 14 or more and a score of 4 on any of the individual items. Thus, when a patient rates as very severe any of the symptoms evaluated by the MRS, it is almost certain that the total score will be 14 points or more.

The weakness of this study is that it analyses a very subjective factor, which is the perception of the patient about the need to be treated. We analyzed in this study women from 40 years of age because we have previously found that 77.0% of premenopausal women (40–44 years) reported at least one climacteric complaint on the MRS, and 12.9% gave total scores defining the condition as severe (> 16 points) [15]. The strength of the present study lies in the instrument used. Our results can guide the clinician in the indication of the need for therapy in women who have experienced a marked deterioration in their quality of life.

5. Conclusion

An MRS score of 14 or more, and not 17 or more, according to the womańs own perception, indicates the need to receive some therapy to treat climacteric symptoms.

Contributors

Juan Enrique Blümel conceived and designed the experiments, and contributed to data analysis and interpretation, and to the drafting of the manuscript.

Eugenio Arteaga contributed to data analysis and interpretation, and to the drafting of the manuscript.

Joaquín Parra contributed to data collection and analysis.

Carolina Monsalve contributed to data collection and analysis.

Valentina Reyes contributed to data collection and analysis.

María Soledad Vallejo contributed to the data analysis and interpretation, and to the drafting of the manuscript.

Rosa Chea contributed to the data analysis and interpretation, and to the drafting of the manuscript.

Conflict of interest

The authors declare that they have no conflicts of interest, and are responsible alone for the content and writing of this document.

Funding

No funding was received for this study.

Ethical approval

This study was approved by the Comité de Ética del Servicio de Salud Metropolitano Sur, Santiago, Chile, according to the Helsinki Declaration. All participants gave informed consent for the use of their data to perform clinical studies, maintaining confidentiality.

Provenance and peer review

This article has undergone peer review.

Research data (data sharing and collaboration)

The data set will be available from 16 May 2018 at https://data.mendeley.com/datasets/t3t4z976tp/draft?a=adc1a054-caf7-40be-9ce1-e5ad46417221

References

[1] The North American Menopause Society, POSITION STATEMENT. The 2017 hormone therapy position statement of the North American menopause society, Menopause 24 (2017) 728–753.

[2] T.J. de Villiers, J.E. Hall, J.V. Pinkerton, S.C. Pérez, M. Rees, C. Yang, D.D. Pierroz, Revised global consensus statement on menopausal hormone therapy, Maturitas 91 (2016) 153–155.

[3] C. Acquadro, R. Berzon, D. Dubois, N.K. Leidy, P. Marquis, D. Revicki, PRO Harmonization Group, 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 6 (2003) 522–531.

[4] National Institute for Health and Clinical Excellence. Clinical Guideline 44; Heavy menstrual bleeding (Last updated: August 2016). Available at: https://www.nice.org.uk/guidance/cg44. [October 2, 2017].

[5] K. Heinemman, A. Ruebig, P. Potthof, The menopause rating scale (MRS): A methodological review, Qual. Life Res. 2 (2004) 45.

[6] N. Santoro, K. Sutton-Tyrrell, The SWAN song: study of women's health across the nation's recurring themes, Obstet. Gynecol. Clin. North Am. 38 (2011) 417–423.

[7] K.M. Brett, Y. Chong, Hormone Replacement Therapy: Knowledge and Use in the States United, National Center for Health Statistics, Hyattsville, Maryland, 2001.

[8] M. del Prado, A. Fuenzalida, D. Jara, R. Figueroa, D. Flores, J.E. Blumel, Assessment of quality of life using the Menopause Rating Scale in women aged 40 to 59 years, Rev. Med. Chil. 136 (2008) 1511–1517.

[9] DEIS. Ministerio de Salud. Chile Población por sexo, según Servicio de Salud y Comuna. Región Metropolitana de Santiago. Available at: http://deis.minsal.cl/deis/pob2010/Region_XIII.htm. October, 4, 2017.

[10] S. Aedo, A. Porcile, C. Irribarra, Calidad de vida relacionada con el climaterio en una población chilena de mujeres saludables, Rev. Chil. Obstet. Ginecol. 71 (2006) 402–409.

[11] M. Szklo, F.J. Nieto, Epidemiology Beyond the Basics, ASPEN Publishers, Inc, Gaithersburg, MD, 2000.

[12] N.J. Perkins, E.F. Schisterman, The inconsistency of "optimal" cutpoints obtained using two criteria based on the receiver operating characteristic curve, Am. J. Epidemiol. 163 (2006) 670–675.

[13] World Medical Association, Declaration of Helsinki. Recommendations guiding physicians in biomedical research involving human subjects, JAMA 277 (1997) 925–926.

[14] The Berlin Center for Epidemiology and Health Research (ZEG). MRS – The Menopause Rating Scale. Available at: http://www.menopause-rating-scale.info/documents/Ref_Values_CountrGr.pdf [October 17, 2017].

[15] J.E. Blümel, P. Chedraui, G. Baron, E. Belzares, A. Bencosme, A. Calle, Collaborative Group for Research of the Climacteric in Latin America (REDLINC), et al., Menopausal symptoms appear before the menopause and persist 5 years beyond: a detailed analysis of a multinational study, Climacteric 15 (2012) 542–551.

[16] F. Légaré, M.H. Brouillette, Shared decision-making in the context of menopausal health: where do we stand, Maturitas 63 (2009) 169–175.

[17] National Institute for Health and Clinical Excellence, NICE Guideline [NG23]; Menopause: Diagnosis and Management, (2015) (November). Available at: https://www.nice.org.uk/guidance/ng23/chapter/Recommendations#individualised-care. [October 17, 2017].

[18] J. Dinger, L.A.J. Heinemann, Menopause Rating Scale as Outcome Measure for Hormone Treatment, Congress of the International Society of Pharamacoepidemiology (Poster), Nashville, U.S.A, 2017, p. 17 (Available at: https://www.nice.org.uk/guidance/ng23/chapter/Recommendations#individualised-care [October 17, 2017]).

[19] N. Chuni, C.T. Sreeramareddy, Frequency of symptoms, determinants of severe symptoms, validity of and cut-off score for Menopause Rating Scale (MRS) as a screening tool: a cross-sectional survey among midlife Nepalese women, BMC Womens Health 14 (11) (2011) 30, http://dx.doi.org/10.1186/1472-6874-11-30.