

Original article

Menopause-related symptoms and quality of life in peri- and postmenopausal women in Thailand: a multicenter study

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Background: Menopausal symptoms can affect the quality of life (QoL) of women.

Objectives: To determine menopause-related symptoms and QoL in peri- and postmenopausal women in Thailand undergoing various treatment.

Methods: A prospective cohort study was conducted at 9 menopause clinics in 4 regions of Thailand. Peri- and postmenopausal women newly registered at the clinics were recruited and followed up for 12 months. A standardized medical record form was used to collect data regarding demographic characteristics, menopause-related symptoms, and treatment. QoL was evaluated using a specific questionnaire.

Results: We included 870 women who were 51.8 ± 5.6 years old. We compared demographic characteristics and baseline health profiles of women with normal QoL and impaired QoL. Women with impaired QoL were significantly younger (51.2 ± 4.4 vs. 52.0 ± 6.0 y, $P = 0.035$) and included more from northeast Thailand (11.4% vs. 6.6%, $P = 0.022$). The 3 most common menopause-related symptoms were psychoemotional distress, musculoskeletal pain, and hot flushes. All QoL scores improved with time in both users and nonusers of postmenopausal hormone therapy (pHT), and the scores of both groups converged during months 3 to 12 of the follow-up period.

Conclusions: The most common menopause-related symptom in peri- and postmenopausal women in Thailand is psychoemotional distress. QoL scores of women with moderate-to-severe menopause-related symptoms at baseline improve over time, whether or not they use of pHT. The pHT users had poorer QoL at baseline than nonusers, but their QoL improves and matches that of their peers after 3 months.

Keywords: Hormonal therapy, menopause-related symptoms, quality of life

Menopause is a state of physiological change in response to the cessation of ovarian function. Despite this, women approaching menopause encounter various health problems including menopause-related problems and age-related diseases. These health problems

adversely affect women's quality of life (QoL) [1]. In 1994, the International Conference on Population and Development (ICPD) recommended that each country should provide comprehensive reproductive health services for people of all ages [2]. For women's health, menopause is among the most important issues because of the increase in life expectancy, most women live one-third of their life after menopause [3].

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Various aspects of menopause have been extensively investigated to understand menopause better and to determine effective management strategies. By the end of 20th century, there were a considerable number of publications, from basic molecular research to epidemiologic studies and clinical trials, contributing to the current management guidelines for menopausal women. Notable studies, in the order of their commencement, include the Nurses' Health Study, the Postmenopausal Estrogen/Progestin Interventions (PEPI) trial, the Heart and Estrogen/Progestin Replacement Study (HERS), the Women's Health Initiative (WHI) study [4], the Million Women Study, and the E3N cohort study [5]. The North American Menopause Society in 2012 [6] and the International Menopause Society (IMS) in 2011 [7] recommended that the most effective treatment for menopause-related problems is postmenopausal hormone therapy (pHT), which is indicated for the treatment of vasomotor symptoms and urogenital atrophy, and for the prevention and treatment of postmenopausal osteoporosis. In addition, they introduced the "Window of Opportunity" concept, which suggests the benefit of pHT in early postmenopausal women (i.e. when women are younger than 60 years old or have undergone menopause for less than 10 years). The concept suggests that the lowest effective dose of pHT should be initiated during the early postmenopausal period, when pHT is considered safe, and might be beneficial for cardio protection.

Despite a lot of evidence, repeated studies of menopause issues in different populations using proper research methodology are still of value in adding more scientific knowledge, as the magnitude of problems and the response to treatment might vary between different populations because of differences in genetic predisposition, environmental factor, culture, and socioeconomic status. Previous studies of the Thai population were mostly conducted at single institutes including only a certain group of the population, which might not well represent the entire Thai population. Moreover, after the first report of the WHI study, which created pHT phobia in the early 21st century, the behavior of menopausal women seeking treatment might be changed and worth evaluating. In the present report, we conducted a multicenter study of peri- and postmenopausal women in Thailand who were not receiving treatment for menopause-related problems and newly registered to menopause clinics, to

determine the prevalence of menopause-related symptoms, the response to treatment, and their QoL during the first year follow-up period.

Materials and methods

A prospective cohort study was conducted between November 2010 and October 2012 at 9 menopause clinics of medical institutes in 4 regions of Thailand, i.e. *the central region* (5 clinics (i) the Phramongkutkloa College of Medicine and Hospital, (ii) the Faculty of Medicine Siriraj Hospital, Mahidol University, (iii) the Bangkok Metropolitan Administration Medical College, Vajira Hospital, (iv) the Faculty of Medicine, Thammasat University, and (v) the Police General Hospital); *the northern region* (2 clinics (i) Faculty of Medicine, Chiang Mai University, and (ii) the Faculty of Medicine, Naresuan University); *the southern region* (one clinic at the Faculty of Medicine, Prince of Songkla University); and *the northeastern region* (one clinic at the Faculty of Medicine, Khon Kaen University). The study protocol was approved by the institutional review board of each institute.

Participants were Thai women who were at least 40 years old and presented with menopause-related symptoms, excluding those who were using hormones within 3 months before participating in the study, could not communicate, or had severe medical diseases such as kidney impairment, immunodeficiency, or cardiovascular disease.

The participants were informed regarding the study procedures. A written informed consent was obtained before their enrollment in the present study. A structured record form was used to collect clinical data. Data collected at the first visit included demographic data, complaints, medical history, physical and per-vaginal examinations, and blood tests for health surveillance (i.e. fasting blood sugar, blood urea nitrogen, creatinine, cholesterol, triglyceride, high-density lipoprotein cholesterol (HDL), low-density lipoprotein cholesterol (LDL). Mammography or bone mineral density (BMD) was measured as indicated by clinical findings. The participants then answered two QoL questionnaires. The choice of treatment for menopause-related symptoms was based on the agreement between the patients and their gynecologists. The patients were then appointed for follow-up visits at 3, 6, and 12 months. At each visit, the data recorded were menopause-related symptoms, medications, and QoL.

Menopause-related symptoms

The present study used the international version of the menopause rating scale (MRS) [8] to categorize the severity of menopause-related symptoms. The questionnaire includes 24 topics including vasomotor, psychological, musculoskeletal, skin and mucous membranes, urinary, and genital symptoms. In each topic, the score is 0 to 3. The total score is classified in 3 groups of severity: 18–24, mild; 25–48, moderate; and 49–72, severe symptoms.

QoL evaluation

QoL was evaluated using 3 questionnaires including the Menopause-Specific Quality of Life Questionnaire (MENQOL) [9], the European QoL-5 Dimensions (EQ-5D) [10], and the Short Form Health Survey 36 (SF-36) [11]. The MENQOL is a menopause-specific 4-dimension QoL questionnaire evaluating vasomotor, psychosocial, physical, and sexual domains using numeric rating scale of 1–8, where 1 represents no symptoms and 8 represents the most severe symptom greatly affecting daily life. In the present study, a MENQOL score of 4 (third quartile) was used as the cutoff to categorize the participants into 2 groups, i.e. normal QoL (MENQOL <4) and impaired QoL (MENQOL ≥4). The EQ-5D is a tool to evaluate general health status comprising 5 dimensions, viz. movement, self-care, daily activity, pain or discomfort, and anxiety or depression. The EQ-5D scores range from 0 (worst) to 100 (best). The SF-36 is a general health questionnaire measuring 2 health domains, which are physical and mental health. It consists of 36 questions that cover 8 dimension profiles of functional health and well-being scores. The physical health domain comprises physical functioning, role limitations because of physical problems, bodily pain, and general health dimensions. The mental health domain comprises vitality, social functioning, role limitations because of emotional problems and general mental health dimensions [11].

Statistical analysis

Statistical analysis was conducted using STATA/MP (version 12; StataCorp, College Station, TX, USA). Data are presented in mean ± standard deviation (SD), or number (n) and percent (%) as appropriate. Data were analyzed using univariate analyses to survey potential predictors for the impaired QoL, and multiple logistic regression analysis to

identify the significant independent predictors. Univariate analyses were conducted using a Student *t* test or Mann–Whitney *U* test (for continuous data), or Chi-square test or Fisher exact test (for categorical data). Multiple regression analyses were conducted using the entering method. Repeated measures analysis of covariance (ANCOVA) was used to compare the change in QoL between the users and nonusers of pHT. All statistical tests were two-tailed and a *P* < 0.05 was considered significant.

Results

Table 1 demonstrates sociodemographic characteristics of 870 peri- and postmenopausal Thai women. The majority of participants were from central region of Thailand, had >12 years education, were still working, had middle-to-upper income (15,000 to 49,999 baht/month or approximately 6,000 to 20,000 USD/year), 75.3% were married and 79.7% were without children. Factors significantly affecting QoL were region of residence and marital status. When comparing the difference between the normal and the impaired QoL group, the women from northeast Thailand had significantly higher score differences. Smaller score differences were found in women from central Thailand and single women, but were higher in divorced women.

Table 2 demonstrates baseline health profiles of the participants. Most participants were older than 45 years, had a BMI ≥23 kg/m², and were postmenopausal. Diseases were prevalent in more than half of the participants; the 3 most common were hypertension, bone and joint diseases, and dyslipidemia. The prevalence of impaired metabolic profiles included fasting blood glucose >100 mg/dL, HDL <50 mg/dL, triglyceride ≥150 mg/dL in about a fifth to a third of participants. Prevalent fracture was found in a tenth of the participants; the most common site being the wrist. BMD showed osteoporosis at lumbar spine in 7.1% of 183 participants and at the femoral neck in 1.7% of 178 participants who underwent BMD testing. A Breast Imaging-Reporting and Data System (BI-RADS) IV mammography (suspicious or indeterminate abnormality) was found in 8.3% of 108 women undergoing screening mammography. Of 870 women, 245 (28.2%) were considered having impaired QoL. Age was the only significant factor affecting QoL; women with impaired QoL were younger than those with normal QoL. There was a statistically significant association between the QoL levels

categorized by a MENQOL score at a cutoff of 4 and the scores of the other two QoL tools, i.e. the EQ-5D and SF-36.

Multiple logistic regression analysis was performed by entering the significant factors in **Table 1** and **2** (region of residence, marital status, and age (<45 vs ≥45 years). We found that region of residence and marital status significantly affect QoL in this Thai population ($P = 0.032$ and 0.001 , respectively).

Table 3 demonstrates prevalence of menopause-related symptoms. We found that 78.7% (95%CI 75.9–81.4) of the participants had at least one symptom. The most common symptoms were nonspecific to a hypoestrogenic state; these included psychoemotional distress and musculoskeletal pain, which were found in more than 70% of the participants. The symptoms specifically related to a

hypoestrogenic state including hot flushes and urogenital symptoms were found in <70% of the participants.

Table 4 presents the QoL at baseline and types of treatment initiated during the first year of follow-up period in 276 women with moderate-to-severe menopause-related symptoms. The most common treatment was non-pHT.

Figure 1 depicts the change in QoL scores of 156 women with moderate-to-severe menopause-related symptoms during the first year in menopause clinics. At baseline, all QoL scores of the pHT users were significantly poorer than those not using pHT, except for the poorer MENQOL score, which was not significantly different. All QoL scores improved with time. After 3 months, there was no significant difference in any QoL score between the users and the nonusers of pHT.

Table 1. Sociodemographic characteristics.

	All		Normal QoL		Impaired QoL		P
	N	n (%)	N	n (%)	N	n (%)	
Regions of residence	870		625		245		0.007
- Central		484 (55.6)		368 (58.9)		116 (47.4)	0.04
- North		217 (24.9)		145 (23.2)		72 (29.4)	0.10
- Northeast		69 (7.9)		41 (6.6)		28 (11.4)	0.02
- South		100 (11.5)		71 (11.4)		29 (11.8)	0.85
Education (y)	869		624		245		0.18
- <7		172 (19.8)		123 (19.7)		49 (20.0)	
- 7 to 12		133 (15.3)		87 (13.9)		46 (18.8)	
- >12		564 (64.9)		414 (66.4)		150 (61.2)	
Occupational status	826		600		226		>0.99
- Working		677 (82.0)		492 (82.0)		185 (81.9)	
- Housewife		123 (14.9)		89 (14.8)		34 (15.0)	
- Retired		26 (3.2)		19 (3.2)		7 (3.1)	
Incomes (baht/month)	822		596		226		0.14
- <15,000		287 (34.9)		196 (32.9)		91 (40.3)	
- 15,000–49,999		457 (55.6)		342 (57.4)		115 (50.9)	
- >50,000		78 (9.5)		58 (9.7)		20 (8.9)	
Marital status	866		622		244		0.003
- Single		104 (12.0)		87 (14.0)		17 (7.0)	0.007
- Married		652 (75.3)		466 (74.9)		186 (76.2)	0.84
- Divorce		110 (12.7)		69 (11.0)		41 (16.8)	0.03
Nulliparous	870	693 (79.7)	625	485 (77.6)	245	208 (84.9)	0.28
Cigarette smoking	870	4 (0.5)	625	3 (0.5)	245	1 (0.4)	0.89

Data are number and percent (%). Data were analyzed using a Chi-square or Fisher exact test. QoL, quality of life; Impaired QoL, Menopause-Specific Quality of Life Questionnaire (MENQOL) score of ≥4; Normal QoL, MENQOL score of <4

Table 2. Baseline health profiles and quality of life scores

	All		Normal QoL		Impaired QoL		P
	N	Mean ± SD or n (%)	N	Mean ± SD or n (%)	N	Mean ± SD or n (%)	
Age (years)	851	51.8±5.57	607	52.0±6.00	244	51.2±4.40	0.035
- ≥45		792 (93.1)		558 (91.9)		234 (95.9)	0.039
Body mass index (kg/m ²)	858	24.2±3.86	613	24.1±3.8	245	24.5±4.1	0.14
- ≥23		503 (58.6)		357 (58.2)		146 (59.6)	0.34
Waist circumference (cm)	862	79.1±9.96	621	78.9±9.5	241	79.6±11.2	0.38
- >80		359 (41.6)		255 (41.1)		104 (43.2)	0.58
Menopausal status	610		410		200		0.05
- Perimenopausal		212 (34.8)		144 (35.1)		68 (34.0)	
- Natural menopause		186 (30.5)		122 (29.8)		64 (32.0)	
- Surgical menopause		212 (34.8)		144 (35.1)		68 (34.0)	
Duration of menopause >5 y	604	248 (41.1)	410	188 (45.9)	200	60 (30.0)	0.06
Presence of moderate-to-severe menopause-related symptoms	870	276 (31.7)	625	94 (15.0)	245	182 (74.3)	<0.001
Presence of medical diseases*	870	532 (61.2)	625	372 (59.5)	245	160 (65.3)	0.11
- Diabetes mellitus	532	40 (7.5)	372	30 (8.1)	160	10 (6.3)	0.65
- Hypertension	532	144 (27.1)	372	99 (26.6)	160	45 (28.1)	0.37
- Heart disease	532	13 (2.4)	372	10 (2.7)	160	3 (1.9)	0.68
- Dyslipidemia	532	98 (18.4)	372	67 (18.0)	160	31 (19.4)	0.42
- Bone and joint diseases	532	126 (23.7)	372	88 (23.7)	160	38 (23.8)	0.59
- Others	532	120 (22.6)	372	84 (22.6)	160	36 (22.5)	0.64
Presence of previous fracture	870	94 (10.8)	625	68 (10.9)	245	26 (10.6)	0.12
- Wrist	94	86 (91.5)	68	61 (89.7)	26	25 (96.2)	0.84
- Femoral neck	94	19 (20.2)	68	14 (20.6)	26	5 (19.2)	0.86
- Spine	94	12 (12.8)	68	10 (14.7)	26	2 (7.7)	0.37
Fasting blood glucose (mg/dL)	636	94.7±28.7	443	93.7±13.1	193	97.1±48.2	0.18
- >100		130 (20.4)		85 (19.2)		45 (23.3)	0.49
Cholesterol (mg/dL)	645	215.1±45.8	454	214.7±47.4	191	216.0±42.0	0.75
- ≥200		399 (61.9)		277 (61.0)		122 (63.9)	0.50
LDL (mg/dL)	556	134.6±40.3	387	134.8±41.3	387	134.3±38.2	0.89
- ≥160		125 (22.5)		86 (22.2)		39 (10.1)	0.82
HDL (mg/dL)	575	60.02±26.56	401	60.4±30.0	174	59.1±16.0	0.58
- <50		171 (29.7)		115 (28.7)		56 (32.2)	0.40
Triglyceride (mg/dL)	639	111.4±63.6	451	108.6±53.5	188	118.2±82.7	0.083
- ≥150		130 (20.3)		92 (20.4)		38 (20.2)	0.96
Bone mineral density T-score <-2.5 SD							
- Spine	183	13 (7.1)	123	8 (6.5)	60	5 (8.3)	0.24
- Femoral neck	178	3 (1.69)	120	2 (1.67)	58	1 (1.72)	0.57
BI-RADS IV mammography	108	9 (8.33)	74	6 (8.11)	34	3 (8.82)	0.83
QoL scores							
- MENQOL	870	3.34±1.24	625	2.71±0.70	245	4.95±0.80	NA
- EQ-5D	865	0.76±0.16	621	0.80±0.12	244	0.66±0.20	<0.001
- SF-36	870	61.3±16.17	625	48.4±14.87	245	16.4±13.64	<0.001

Data were analyzed using a Student *t* test (for continuous data), or Chi-square or Fisher exact test (for categorical data).

*Each woman might have more than one disease.

BI-RADS, Breast Imaging-Reporting and Data System; EQ-5D, European QoL-5 Dimensions; HDL, high-density lipoprotein; LDL, low-density lipoprotein; MENQOL, Menopause-Specific Quality of Life Questionnaire; pHT, postmenopausal hormone therapy; QoL, quality of life (Impaired QoL = MENQOL score ≥4, Normal QoL = MENQOL score <4), SF-36, Short Form Health Survey 36; NA = not available

Table 3. Prevalence of menopause-related symptoms in peri- or postmenopausal Thai women

Symptoms	n	% (95%CI)
Psychoemotional distress		
- Moody	685	78.7 (75.9–81.4)
- Insomnia	623	71.6 (68.5–75.6)
- Headache	620	71.3 (68.1–74.3)
- Loss of libido	590	69.2 (65.9–72.3)
- Fatigue	580	66.7 (63.4–69.8)
- Depression	367	42.2 (38.9–45.5)
Musculoskeletal pain		
- Joint pain	678	78.0 (75.1–80.7)
- Muscle strain	676	77.8 (74.9–80.5)
- Back pain	661	76.1 (73.1–78.9)
Hot flushes	579	66.6 (63.1–69.7)
Skin dryness	556	64.0 (60.7–67.2)
Urogenital symptoms		
- Vaginal dryness	539	62.7 (59.4–66.0)
- Dyspareunia	457	55.2 (51.7–58.6)
- Urinary incontinence	408	46.9 (43.5–50.3)
- Urinary frequency	321	36.9 (33.7–40.2)
- Dysuria	251	28.9 (25.9–32.0)

Table 4. Quality of life at baseline and types of treatment initiated during the first year of follow-up period in 276 women with moderate-to-severe menopause-related symptoms

	N	Mean \pm SD or n (%)
QoL scores at baseline		
MENQOL	276	4.51 \pm 1.14
EQ-5D	276	0.67 \pm 0.20
SF-36	276	51.01 \pm 15.58
Physical health	276	51.26 \pm 18.72
Mental health	276	50.61 \pm 14.89
Treatments		
pHT	229	27 (11.8)
non-pHT	229	106 (46.3)
SSRI/SNRI	106	12 (11.3)
Herbal products	106	83 (78.3)
Vitamin and calcium	106	3 (2.8)
Others	106	49 (46.2)
Combined therapy	229	96 (41.9)

MENQOL, Menopause-Specific Quality of Life Questionnaire; EQ-5D, European QoL-5 Dimensions; SF-36, Short Form Health Survey 36; pHT, postmenopausal hormone therapy; SSRI, selective serotonin reuptake inhibitor; SNRI, Serotonin–norepinephrine reuptake inhibitor

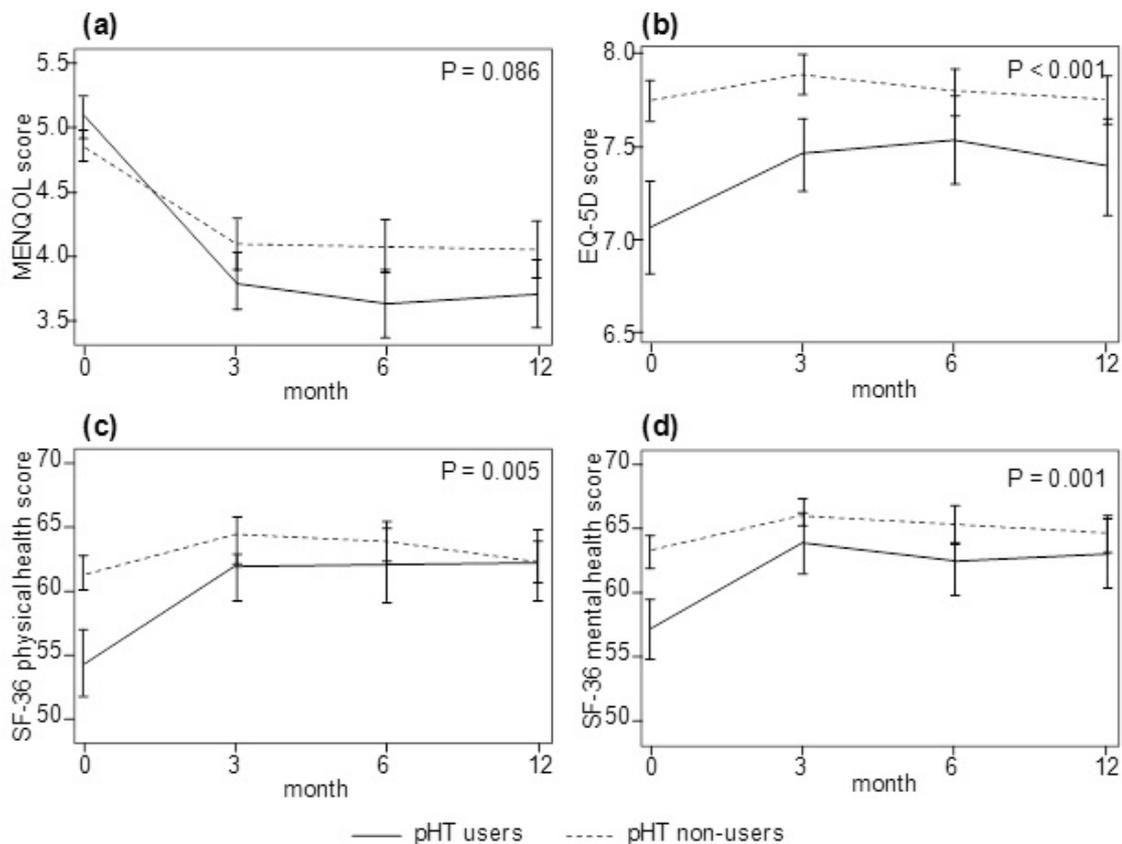


Figure 1. Change in quality of life (QoL) scores of the women with moderate-to-severe menopause-related symptoms during the first year in menopause clinics: (a) Menopause-Specific Quality of Life Questionnaire (MENQOL), (b) European QoL-5 Dimensions (EQ-5D), (c) Short Form Health Survey 36 (SF-36) physical health domain, (d) SF-36 mental health domain. Data are mean and standard deviation. Data were analyzed using repeated measures analysis of covariance (ANCOVA). pHT, postmenopausal hormone therapy

Discussion

The present multicenter prospective cohort study in Thailand demonstrated characteristics, QoL and menopause-related symptoms (both prevalence and therapeutic measures) of peri- or postmenopausal women newly registered to menopause clinics during the early 2010s, approximately 10 years after the first report of WHI study, a landmark randomized-controlled trial of pHT. The overall characteristics of participants in the present study were middle-aged, about 52 years, nearly the average age of menopause in the United States of America, which is 51 years [12]. The present study found (from multiple logistic regression analysis) that region of residence and marital status were independence factors for QoL. Women living in central Thailand and married women had highest impairment of QoL. This finding supported

that city life and family responsibility might impact QoL. Previous studies had found similar trends [13-15]. History of bone fracture was observed about 10% of participants, but with no record of the exact causes of fracture. There is a possibility that fractures might be associated with the menopause. Only some participants tested for BMD showed osteoporosis. The reasons for this finding might be the younger and healthy participants in this study population. The greatest menopause-related symptom was unstable mood at almost 80%; and 42% reported being disturbed with a depressed mood. Many studies reported mood symptoms as a menopause-related symptom during menopausal transition [16, 17]. For perimenopausal women, the prevalence of depressed mood ranges from 11% to 46% [16]. Depression and

anxiety are symptoms with the strongest associations with health outcomes [18]. The results of this study were consistent with previous studies in different populations. The important symptom in this period was hot flushes or climacteric symptoms. The present study found that 66.6% of participants were distressed by this symptom. Previous studies reported the prevalence of climacteric symptoms ranging from 14%–51% and 50% occurred during the perimenopausal period [19, 20]. The present study found higher prevalence of these specific symptoms than previous studies. Vaginal dryness is one of the common concerns in menopause. The present study reported 62.7% suffered this symptom, 55.2% had dyspareunia, and 69.2% had loss of libido. Previous studies reported the prevalence of vaginal dryness at 7%–39% for perimenopausal women, and 17%–30% for early postmenopausal women [20, 21]. Our present study revealed a higher rate for this symptom, possibly because the socioeconomic status of women in Thailand induces psychological problems in sexual life, then leading to loss of libido. Sociodemographic characteristics, lifestyle, and concomitant health problems appear to be important modifiable determinants for menopause-related symptoms. Another factor could be from the partner's sexual desire: men might not lose libido as much as women. Thus, mismatched sexual desire might affect sexual activity.

pHT is an effective treatment for menopause-related symptoms [6]. Furthermore, pHT can improve the QoL of symptomatic menopausal women [22]. Overall QoL in the group of women with menopause-related symptoms and receiving hormonal therapy was better than in the group without treatment with pHT in either the EQ-5D or SF-36 score since the 3rd month of their treatment. Hormonal therapy can improve the QoL in postmenopausal women significantly [23, 24]. The effect of pHT on QoL among postmenopausal women has been studied in the PEPI trial in the United Kingdom, and in the WHI trial in the United States of America [25–27]. All of these trials found advantages of the hormone therapy on vasomotor symptoms. Whereas the present study found improvement of overall general QoL scores, it did not find a significantly better score for specific symptoms (MENQOL score). It may be that Thai women had more nonspecific than specific menopausal symptoms. Therefore, hormonal therapy may improve perceived QoL.

A strength of this study is its multicenter nature, studying each region in Thailand. The present study used specific questionnaires to evaluate the QoL in menopausal transition periods and studied QoL in general. In addition, our prospective cohort study used a one year follow-up, being longer than that of other reports of menopause in Thailand. However, the present has some limitations. The data was collected in medical schools and tertiary hospitals. In this way, the participants might mainly reside in urban areas of each region in Thailand and not truly reflect the general health status of menopausal Thai women nationwide.

The results of this study provide data regarding overall baseline characteristic, menopause-related symptoms, hormonal therapy, and specific QoL data during the menopausal transitional period in Thai women. This may provide insights into the symptoms of menopause to health providers and encourage a holistic approach to these women. The data can be used as a reference for research of women's health.

Contributions

SP, TW, PB, and MR made substantial contributions to the conception and design of the study. All authors made substantial contributions to the acquisition, analysis, and interpretation of data. All authors helped to draft the manuscript; and SP, TW, and MR critically revised it. All authors approved the final version submitted for publication and take full responsibility for its content.

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Conflict of interest

The authors report no conflicts of interest.

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