

# Menopausal Symptoms and Associated Social and Environmental Factors in Midlife Chinese Women

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**Objective:** To investigate the dependency of menopausal symptoms on age and/or menopausal status and association with social and environmental factors.

**Methods:** The cross-sectional study was conducted on 4595 women (40–83 years) coming from 31 provinces during two years to our “Menopause Clinic”, the first official center in China. Menopausal symptoms were assessed: negative mood, cognitive symptoms, sleep disorder, vasomotor symptoms (VMS), urogenital symptoms, autonomic nervous disorder, limb pain/paresthesia. Social and environmental factors were collected; simple and unconditional logistic regression with adjustments by all analyzed factors were used to assess associations.

**Results:** Urogenital symptoms were the most common and VMS the least common complaints. All symptoms, except cognitive and urogenital symptoms, worsened age-dependently up to 60 years but improved beyond this age. Most symptoms also were associated with menopause, except negative mood and autonomic nervous disorders. Soya-rich diet decreased all symptoms, but only if consumed daily. Exercise was beneficial for some symptoms. Hormone replacement therapy (HRT) was most effective but only with regular use. Increased alcohol consumption aggravated VMS. Higher education was associated with less symptoms; no relationship was found for smoking, gravidity, parity, and menarche.

**Conclusion:** All symptoms, except cognitive and urogenital symptoms, worsened age-dependently up to 60 years but improved beyond this age; most were also associated with menopause. For the first time in a large study population, it was observed that soy-rich diet is protective but only with daily consumption. Exercising can protect against some of the symptoms. HRT decreased all symptoms, but regular use is necessary. Women with higher education reported less symptoms, but after adjustments no other relationships were observed (ChiCTR2000035047).

**Keywords:** menopausal symptoms, age, menopause, HRT, associated factors

## Introduction

Menopause marks the end of a woman's reproductive life and is caused by reduced secretion of ovarian hormones.<sup>1</sup> With increased life expectancy, it is estimated that the number of postmenopausal women worldwide will reach 1.1 billion by 2025.<sup>2</sup> Many symptoms have been attributed to menopause, with substantial effects on quality of life.<sup>3</sup> Severe vasomotor symptoms (VMS) and sleep disorders might increase cardiovascular risk; severe VMS and depression may affect cognitive function.<sup>3</sup> On average, menopausal symptoms appear between age 48 and 55 years of age, with menopausal transition typically lasting four to eight years.<sup>4</sup> However, geographical location, ethnicity, education and lifestyle may influence

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the prevalence of menopausal symptoms.<sup>5</sup> Thus, identifying the factors associated with menopausal symptoms, especially those which are modifiable, may be important to reduce the risk of future chronic illness among postmenopausal women. Smoking has been proved to be linked to depressive mood during the menopausal transition.<sup>6</sup> However, the effect of other potential factors involving level of education, lifestyle behavior and soya intake on menopausal symptoms has been studied less, with no universal consensus, and only a few studies have been conducted in Chinese women. In this study, we observed how menopausal symptoms change with age and menopausal status, and examined the association between menopausal symptoms and socio-demographic and environmental factors including treatment possibilities in a large population of midlife women coming from 31 provinces of China to one center, specialized in menopausal issues.

## Participants and Methods

### Patients and Study Design

This cross-sectional study to analyze baseline information was conducted at the Department of Gynecological Endocrinology in the Beijing Obstetrics and Gynecology Hospital, Capital Medical University, China. In total, 4595 outpatient women who visited our new “Menopause Clinic Center” because of menopausal concerns over a 24-month period met the inclusion and exclusion criteria of a validated questionnaire survey and all attended standardized menopausal examinations, including 2407 perimenopausal (52.38%) and 2188 postmenopausal women (47.62%).

All participants provided written informed consent according to the Declaration of Helsinki, and the study was approved by the Ethics Committee of the Beijing Obstetrics and Gynecology Hospital, Capital Medical University, China (2020-KY-008-01).

### Inclusion and Exclusion Criteria

Women were included based on the “2011 Stages of Reproductive Aging Workshop (STRAW+10) staging system”<sup>7</sup> Inclusion criteria: (1) Perimenopause: irregular menstrual cycles, with/without perimenopausal symptoms, (2) Postmenopause:  $\geq 12$  consecutive months without spontaneous menstruation, or bilateral ovariectomy  $\geq 6$  weeks before enrollment (with or without hysterectomy), FSH  $> 40$  IU/L.

Exclusion criteria: (1) prior/current DSM-5 depression, anxiety, sleep or circadian disorders (other than insomnia), Alzheimer’s disease and other mental illness diagnosed by a neurologist; (2) heart disease, (3) Meniere’s disease; (4) joint pain caused by systemic lupus erythematosus or rheumatoid arthritis.

## Assessment of Basic Characteristics, Exposure Variables and Menopausal Symptoms

Certified medical staff collected information on general socio-demographic data using a laptop-based questionnaire (age, nationality, district, marital status), dietary habits (especially consumption of soya products), lifestyle (daily exercise, alcohol, smoking), level of education, HRT, and reproductive characteristics (age at menarche, gravidity, parity). In addition, body weight, height and BMI were assessed, and physicians performed the usual routine examinations before starting any therapy.

A validated research database<sup>8–10</sup> was used containing questions with seven domains: negative mood, cognitive symptom, sleep disorder, VMS, urogenital symptom, autonomic nervous disorder, limb pain/paresthesia, and each domain included several specific items with more detailed questions. Our results (see [supplementary materials](#)) show excellent internal consistency of this online questionnaire and high criterion validity (Cronbach’s  $\alpha=0.960$ , Guttman split-half coefficient=0.852) (KMO=0.961,  $p<0.001$ ; cumulative %=54.994%). Each question was answered on a 0–4 level of severity: none/little, mild, moderate, and severe (corresponding score 0–3). For example, Women were asked if they had been bothered by hot flashes and/or sweating over the previous 2 weeks, and were requested to classify severity (no, light, moderate and heavy, respectively) and frequency (no, 2 times/day, 3–9 times/day, 10 times/day) with a corresponding score of 0–3, which is the same as improved Kupperman Index. The sum of each item divided by the number of items in each domain was defined as one subject’s domain-specific mean value. Similarly, all the subjects’ mean values are the sum of all subject’s domain-specifics divided by the number of subjects. Thus, higher mean scores are indicative of more severe symptoms. Most patients answered the questions themselves, but also could ask a doctor if help was required.

## Statistical Analysis

Statistical analysis was performed using SPSS 22.0. Normality of distribution was assessed with the one-sample Kolmogorov–Smirnov test. Normal distributed data were presented as the mean standard deviation (SD). The menopausal symptoms were described with mean (M). Age and BMI between the two groups were performed with *T* test; nationality, district, HRT, marital status between the two groups were compared using the chi-square test; level of education between the two groups was compared by rank sum test. Simple and unconditional logistic regression were used to assess the relationship between menopausal symptoms and potential confounding factors with odds ratios (*OR*) and their 95% confidence intervals (*CI*) with adjustments by all analyzed factors were reported. A *p*-value of <0.05 was considered to be statistically significant.

## Results

### Demographic and Menopausal Characteristics of Subjects

The demographic and menopausal characteristics of the subjects are presented in Table 1 comparing perimenopausal and postmenopausal women. Age, level of education, marital status and use of HRT differed significantly between the two groups. There was no significant difference in nationality, district, and BMI between the two groups. Among them, 28% (1307) used HRT at least for six months, the number of hysterectomized women is 215 (16.45%), these women have been treated with estrogen-only, whereby we used oral estradiol, or oral estradiol valerate or transdermal estradiol (patch or gel).

**Table 1** Demographic Characteristics of Perimenopausal and Postmenopausal Women (n=4595)

Item	All Subjects (n=4595)	Perimenopausal (n=2407)	Postmenopausal (n=2188)	Statistics P value
Age <sup>a</sup>	50.69±6.49	48.77±6.15	52.77±6.21	-21.772, 0.000*
Nationality <sup>b</sup>				
Han	3238(70.49%)	1701(70.67%)	1537(70.25%)	1.139,0.286
Non-Han	237(5.16%)	133(5.53%)	104(4.75%)	
Did not answer	1120(24.37%)	573(23.81%)	547(25.00%)	
District <sup>b</sup>				
Beijing	1603(34.89%)	868(36.06%)	735(33.59%)	1.174,0.190
Non-Beijing	281(6.12%)	164(6.81%)	117(5.35%)	
Did not answer	2711(59.00%)	1375(57.13%)	1336(61.06%)	
HRT <sup>b</sup>				
Yes	1307(28.44%)	520(21.60%)	787(35.97%)	83.175, 0.000*
hysterectomized women	215(16.45%)	6(1.15%)	207(26.30%)	
No	2195(47.77%)	1223(50.81%)	972(44.42%)	
Did not answer	1093(23.79%)	664(27.59%)	429(19.61%)	
Medical menopause	-	-	719(32.86%)	-
Natural menopause	-	-	1063(48.58%)	
Did not answer	-	-	406(18.56%)	
Level of education <sup>c</sup>				
Junior high school/below	907(19.74%)	438(18.20%)	469(21.44%)	-4.334, 0.000*
Senior high school	479(10.42%)	239(9.93%)	240(10.97%)	
Technical secondary school	704(15.32%)	338(14.04%)	366(16.73%)	
Bachelor's degree/above	1988(43.26%)	1111(46.16%)	877(40.08%)	
BMI(Kg/m <sup>2</sup> ) <sup>a</sup>	24.19±3.78	24.18±4.20	24.20±3.32	-0.843, 0.399
Marital status <sup>b</sup>				
Married	2468(53.71%)	1223(50.81%)	1245(56.90%)	16.174, 0.000*
Single	1247(27.14%)	705(29.29%)	542(24.77%)	
Did not answer	880(19.15%)	479(19.90%)	401(18.33%)	

**Notes:** Data are expressed as mean ± SD or n (%). <sup>a</sup>Student's test of independent samples (*t*). <sup>b</sup>Pearson Chi-square ( $\chi^2$ ). <sup>c</sup>Rank sum test (*Z*). \**P*< 0.05 is considered statistically significant.

**Abbreviations:** HRT, hormone replacement therapy; BMI, body mass index; *t*, *t*-statistic;  $\chi^2$ , chi-square; *Z*, rank-sum test; *P*, significance value.

## Prevalence of Menopausal Symptoms Comparing Perimenopausal and Postmenopausal Women

As shown in Figure 1, the prevalence of urogenital symptoms was the highest (97.92%) and VMS was the lowest (48.83%) within our patient sample.

## Changes in Menopausal Symptoms with Age

The severity of menopausal symptoms increased with age as shown in Figure 2, but decreased after 60 years of age, with the exception of cognitive and urogenital symptoms. However, because there were only 313 women ≥60 years of age, the results in this age-group are not robust.

## Risk Factors for Menopausal Symptoms

The associations between menopausal symptoms and age, menopausal status, level of education, daily exercise intensity, daily exercise, smoking, alcohol consumption, menarche, gravidity and parity, HRT and consumption of

soya products are presented in Table 2 as crude odds ratio (OR) and adjusted OR. The adjustment was made for each analyzed factor for all items. Because of the very large number of women with urogenital symptoms, there was a lack of control for analyzing multiple regression risk factors with urogenital symptoms; therefore, these complaints are not included in Table 2.

Besides the relationship to age (Figure 2), menopausal symptoms also were dependent on menopause, except negative mood and autonomic nervous disorders, which only showed an age-dependent increase (up to 60 years). Proper physical activity was beneficial for controlling negative mood, insomnia, and autonomic nervous disorders, but showed no significant association with VMS, cognitive symptoms and limb pain/paresthesia.

A soya-rich diet could decrease all symptoms, but daily consumption was needed, and less than daily intake was not effective for any symptom. Likewise, HRT could decrease all symptoms, but regular use with daily administration for at least 6 months was necessary. Regarding the association with other factors, only a higher level of

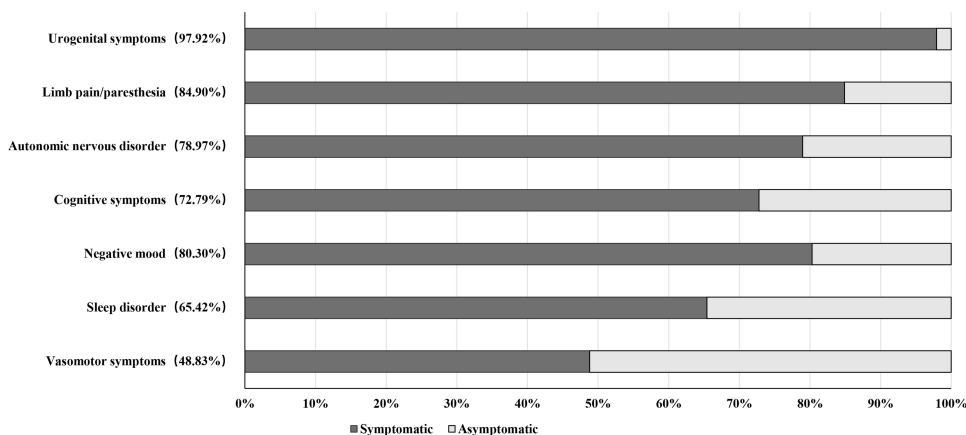


Figure 1 Prevalence of menopausal symptoms in midlife women (n=4595).

Note: Data are expressed as percentage (%).

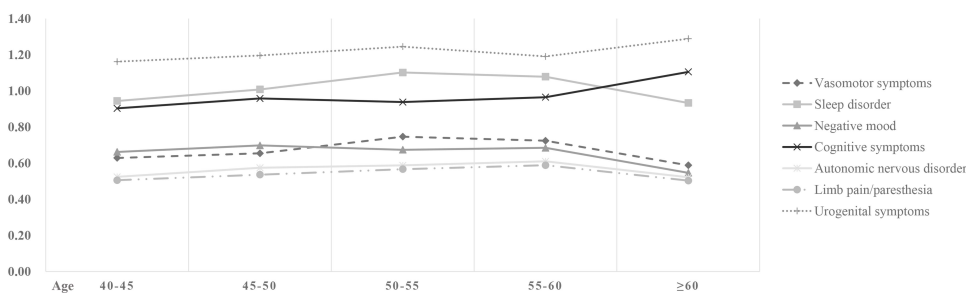


Figure 2 Dependence of the severity of the domain menopausal symptoms on age (n=4595).

Note: Data are expressed as mean score.

**Table 2** Factors Influencing Menopausal Symptoms Analyzed by Simple and Unconditional Logistic Regression Analysis (n=4595)

Menopausal Symptom	Crude OR(95% CI)	P value	Adjusted OR(95% CI)	P value
<b>1) Negative mood</b>				
Menopause or not		0.164		NS
No	1.000			
Yes	1.115(0.956,1.301)	0.164		
Age	1.014(1.002,1.027)	0.018*	1.037(1.023,1.052)	<0.001*
Level of education		<0.001*		<0.001*
Bachelor's degree/above	1.000		1.000	
Senior high school	5.501(4.570,6.621)	<0.001	2.346(1.791,3.072)	<0.001
Technical secondary school	5.218(4.053,6.718)	<0.001	2.407(1.764,3.284)	<0.001
Junior high school/below	7.309(5.277,10.123)	<0.001	3.332(2.288,4.853)	<0.001
Soya product intake		<0.001*		<0.001*
No	1.000		1.000	
3–5 times/week	1.042(0.746,1.456)	0.809	1.187(0.791,1.781)	0.408
2–3 times/week	0.795(0.570,1.110)	0.178	0.904(0.606,1.348)	0.621
1–2 times/week	0.832(0.581,1.190)	0.314	0.845(0.553,1.291)	0.435
≥1 time/day	0.183(0.133,0.253)	<0.001	0.502(0.328,0.769)	0.002
Daily exercise intensity		<0.001*		<0.001*
None	1.000		1.000	
Mild	0.233(0.168,0.324)	<0.001	0.990(0.723,1.354)	0.948
Moderate	0.916(0.652,1.287)	0.613	0.568(0.413,0.782)	0.001
Heavy	1.255(0.885,1.781)	0.202	0.472(0.280,0.797)	0.005
Daily exercise amount		<0.001*		NS
None	1.000			
<30 minutes/day	0.906(0.732,1.123)	0.367		
≥30 minutes/day	0.235(0.194,0.285)	<0.001		
Smoking		<0.001*		NS
No	1.000			
Yes	3.307(2.752,3.975)	<0.001		
Alcohol consumption		<0.001*		NS
No/seldom	1.000			
Often	3.330(2.783,3.983)	<0.001		
HRT		<0.001*		<0.001*
Regularly	1.000		1.000	
Irregularly	3.039(2.262,4.084)	<0.001	2.018(1.455,2.801)	0.029
NO	15.919(2.200,115.186)	0.006	9.265(1.255,68.377)	<0.001
Higher age at menarche	1.025(0.962,1.092)	0.439		NS
Gravidity	0.986(0.907,1.073)	0.750		NS
Parity	1.009(0.807,1.263)	0.935		NS
<b>2) Cognitive symptoms</b>				
Menopause or not		0.010*		0.004*
No	1.000		1.000	
Yes	1.198(1.044,1.375)	0.010	1.302(1.090,1.554)	0.004
Age	1.009(0.998,1.019)	0.111	1.034(1.019,1.049)	<0.001*

(Continued)

Table 2 (Continued).

Menopausal Symptom	Crude OR(95% CI)	P value	Adjusted OR(95% CI)	P value
Level of education		<0.001*		<0.001*
Bachelor's degree/above	1.000		1.000	
Senior high school	5.900(4.962,7.014)	<0.001	2.242(1.755,2.864)	<0.001
Technical secondary school	6.241(4.946,7.875)	<0.001	2.543(1.922,3.364)	<0.001
Junior high school/below	7.022(5.334,9.245)	<0.001	2.875(2.089,3.956)	<0.001
Soya product intake		<0.001*		<0.001*
No	1.000		1.000	
3–5 times/week	0.906(0.677,1.213)	0.509	1.146(0.811,1.620)	0.441
2–3 times/week	0.803(0.597,1.078)	0.144	0.971(0.687,1.372)	0.866
1–2 times/week	0.799(0.583,1.095)	0.163	0.897(0.622,1.295)	0.563
≥1 time/day	0.142(0.106,0.190)	<0.001	0.412(0.283,0.600)	<0.001
Daily exercise intensity		<0.001*		NS
None	1.000			
Mild	1.149(0.849,1.554)	0.369		
Moderate	0.842(0.627,1.132)	0.256		
Heavy	0.219(0.163,0.293)	0.000		
Daily exercise amount		<0.001*		NS
None	1.000			
<30 minutes/day	0.953(0.791,1.148)	0.613		
≥30 minutes/day	0.209(0.175,0.248)	0.000		
Smoking		<0.001*		NS
No	1.000			
Yes	2.949(2.524,3.446)	<0.001		
Alcohol consumption		<0.001*		NS
No/seldom	1.000			
Often	3.051(2.618,3.556)			
HRT		<0.001*		0.001*
Regularly	1.000		1.000	
Irregularly	2.762(2.164,3.524)	<0.001	1.558(1.171,2.074)	0.002
NO	5.705(2.059,15.803)	0.001	3.190(1.117,9.111)	0.030
Higher age at menarche	0.975(0.929,1.024)	0.314		NS
Gravidity	0.983(0.920,1.050)	0.605		NS
Parity	0.893(0.752,1.061)	0.199		NS
<b>3) Sleep disorder</b>				
Menopause or not		0.003*		0.007*
No	1.000		1.000	
Yes	1.215(1.068,1.384)	0.003	1.258(1.092,1.450)	0.007
Age	1.021(1.011,1.031)	<0.001*	1.026(1.013,1.039)	<0.001*
Level of education		<0.001*		<0.001*
Bachelor's degree/above	1.000		1.000	
Senior high school	2.857(2.429,3.362)	<0.001	1.338(1.057,1.694)	0.016
Technical secondary school	3.687(2.974,4.570)	<0.001	1.887(1.144,2.465)	<0.001
Junior high school/below	4.368(3.391,5.625)	<0.001	2.058(1.527,2.775)	<0.001

(Continued)

Table 2 (Continued).

Menopausal Symptom	Crude OR(95% CI)	P value	Adjusted OR(95% CI)	P value
Soya product intake		<0.001*		<0.001*
No	1.000		1.000	
3–5 times/week	1.037(0.808,1.330)	0.777	1.153(0.858,1.549)	0.346
2–3 times/week	0.922(0.716,1.188)	0.531	1.061(0.787,1.429)	0.698
1–2 times/week	0.933(0.710,1.226)	0.618	0.942(0.687,1.291)	0.709
≥1 time/day	0.283(0.218,0.366)	<0.001	0.555(0.396,0.779)	0.001
Daily exercise intensity		<0.001*		<0.001*
None	1.000		1.000	
Mild	1.312(1.104,1.560)	0.002	1.111(0.877,1.407)	0.382
Moderate	1.036(0.799,1.344)	0.789	0.836(0.566,1.235)	0.369
Heavy	0.362(0.306,0.429)	<0.001	0.560(0.430,0.730)	<0.001
Daily exercise amount		<0.001*		NS
None	1.000			
<30 minutes/day	0.910(0.774,1.069)	0.251		
≥30 minutes/day	0.357(0.303,0.420)	<0.001		
Smoking		<0.001*		NS
No	1.000			
Yes	2.254(1.960,2.593)	<0.001		
Alcohol consumption		<0.001*		NS
No/seldom	1.000			
Often	2.143(1.869,2.457)	<0.001		
HRT		<0.001*		0.041*
Regularly	1.000		1.000	
Irregularly	1.477(1.219,1.789)	0.002	1.070(0.341,1.861)	<0.001
NO	3.275(1.541,6.961)	<0.001	1.992(1.910,4.360)	0.041
Higher age at menarche	1.011(0.986,1.055)	0.663		NS
Gravidity	0.989(0.933,1.049)	0.710		NS
Parity	0.945(0.810,1.101)	0.467		NS
<b>4) Vasomotor symptoms</b>				
Menopause or not		<0.001*		0.009*
No	1.000		1.000	
Yes	1.303(1.153,1.474)	<0.001	1.259(1.060,1.495)	0.009
Age	1.021(1.012,1.031)	<0.001*	1.023(1.011,1.036)	<0.001*
Level of education		<0.001*		<0.001*
Bachelor's degree/above	1.000		1.000	
Senior high school	1.753(1.490,2.062)	<0.001	1.016(0.804,1.284)	0.894
Technical secondary school	2.448(2.000,2.997)	<0.001	1.489(1.153,1.922)	0.002
Junior high school/below	2.889(2.295,3.636)	<0.001	1.725(1.305,2.279)	<0.001
Soya product intake		0.002*		<0.001*
No	1.000		1.000	
3–5 times/week	1.833(1.318,2.549)	<0.001	0.826(0.644,1.060)	0.134
2–3 times/week	1.377(1.067,1.777)	0.014	0.775(0.618,0.973)	0.028
1–2 times/week	1.456(1.098,1.931)	0.009	0.675(0.535,0.851)	0.001
≥1 time/day	1.573(1.222,2.026)	<0.001	0.359(0.280,0.460)	<0.001

(Continued)



Table 2 (Continued).

Menopausal Symptom	Crude OR(95% CI)	P value	Adjusted OR(95% CI)	P value
Daily exercise intensity		<0.001*		NS
None	1.000			
Mild	0.900(0.711,1.140)	0.383		
Moderate	0.773(0.611,0.979)	0.032		
Heavy	0.412(0.322,0.526)	<0.001		
Daily exercise amount		<0.001*		NS
None	1.000			
<30 minutes/day	0.841(0.728,0.973)	0.020		
≥30 minutes/day	0.473(0.404,0.553)	<0.001		
Smoking		<0.001*		NS
No	1.000			
Yes	1.644(1.449,1.865)	<0.001		
Alcohol consumption		<0.001*		0.018*
No/seldom	1.000		1.000	
Often	0.675(0.488,0.934)	0.018	1.547(1.365,1.753)	<0.001
HRT		<0.001*		0.001*
Regularly	1.000		1.000	
Irregularly	0.775(0.636,0.945)	0.012	1.187(0.883,1.596)	0.255
NO	1.558(1.242,1.955)	<0.001	1.679(1.281,2.200)	<0.001
Higher age at menarche	1.016(0.978,1.056)	0.410		NS
Gravidity	1.036(0.984,1.091)	0.182		NS
Parity	1.023(0.892,1.174)	0.742		NS
<b>5) Limb pain/paresthesia</b>				
Menopause or not		0.030*		<0.001*
No	1.000		1.000	
Yes	1.209(1.018,1.435)	0.030	1.779(1.296,2.442)	<0.001
Age	1.015(1.001,1.028)	0.029*	1.005(0.982,1.029)	<0.001*
Level of education		<0.001*		0.030*
Bachelor's degree/above	1.000		1.000	
Senior high school	0.795(0.585,1.081)	0.143	1.365(0.958,1.946)	0.085
Technical secondary school	0.110(0.089,0.136)	<0.001	1.493(0.926,2.408)	0.100
Junior high school/below	1.141(0.764,1.704)	0.520	1.803(1.139,2.854)	0.012
Soya product intake		<0.001*		0.002*
No	1.000		1.000	
3–5 times/week	0.704(0.448,1.107)	0.129	1.142(0.702,1.857)	0.549
2–3 times/week	0.554(0.353,0.870)	0.010	0.779(0.484,1.252)	0.302
1–2 times/week	0.540(0.337,0.868)	0.011	0.712(0.433,1.171)	0.180
≥1time/day	0.093(0.061,0.143)	0.000	0.446(0.250,0.797)	0.006
Daily exercise intensity		<0.001*		NS
None	1.000			
Mild	0.194(0.156,0.241)	<0.001		
Moderate	1.487(0.954,2.317)	0.080		
Heavy	1.895(1.410,2.547)	<0.001		

(Continued)



Table 2 (Continued).

Menopausal Symptom	Crude OR(95% CI)	P value	Adjusted OR(95% CI)	P value
Daily exercise amount		<0.001*		NS
None	1.000			
<30 minutes/day	0.171(0.136,0.215)	<0.001		
≥30 minutes/day	1.086(0.832,1.418)	0.542		
Smoking		<0.001*		NS
No	1.000			
Yes	5.771(4.522,7.366)	<0.001		
Alcohol consumption		<0.001*		NS
No/seldom	1.000			
Often	5.860(4.627,7.420)	<0.001		
HRT		<0.001*		<0.001*
Regularly	1.000		1.000	
Irregularly	0.867(0.493,1.525)	0.620	2.068(1.355,3.156)	0.001
NO	0.124(0.078,0.199)	<0.001	2.543(1.542,4.193)	<0.001
Higher age at menarche	0.935(0.861,1.016)	0.113		NS
Gravidity	0.920(0.824,1.026)	0.134		NS
Parity	0.748(0.576,0.973)	0.030*		NS
<b>6) Autonomic nervous disorder</b>				
Menopause or not		0.007*		NS
No	1.000			
Yes	1.230(1.058,1.430)	0.007		
Age	1.019(1.007,1.031)	0.002*	1.041(1.025,1.057)	<0.001*
Level of education		<0.001*		<0.001*
Bachelor's degree/above	1.000		1.000	
Senior high school	4.129(3.456,4.934)	<0.001	2.077(1.594,2.707)	<0.001
Technical secondary school	4.702(3.666,6.031)	<0.001	2.339(1.723,3.176)	<0.001
Junior high school/below	6.392(4.659,8.771)	<0.001	3.205(2.223,4.623)	<0.001
Soya product intake		<0.001*		<0.001*
No	1.000		1.000	
3–5 times/week	1.155(0.842,1.585)	0.371	1.274(0.873,1.859)	0.209
2–3 times/week	0.858(0.626,1.176)	0.341	0.922(0.635,1.338)	0.669
1–2 times/week	0.786(0.563,1.098)	0.158	0.769(0.521,1.136)	0.187
≥1 time/day	0.221(0.163,0.300)	<0.001	0.481(0.322,0.720)	<0.001
Daily exercise intensity		<0.001*		0.001*
None	1.000		1.000	
Mild	1.059(0.854,1.313)	0.602	0.881(0.657,1.182)	0.398
Moderate	0.857(0.627,1.173)	0.336	0.604(0.372,0.979)	0.041
Heavy	0.273(0.225,0.331)	<0.001	0.568(0.414,0.778)	<0.001
Daily exercise amount		<0.001*		NS
None	1.000			
<30 minutes/day	0.886(0.724,1.084)	0.238		
≥30 minutes/day	0.283(0.233,0.343)	0.000		
Smoking		<0.001*		NS
No	1.000			
Yes	2.536(2.141,3.005)	<0.001		

(Continued)

**Table 2** (Continued).

Menopausal Symptom	Crude OR(95% CI)	P value	Adjusted OR(95% CI)	P value
Alcohol consumption		<0.001*		NS
No/seldom	1.000			
Often	2.623(2.220,3.098)	<0.001		
HRT		<0.001*		0.042*
Regularly	1.000		1.000	
Irregularly	0.463(0.356,0.602)	<0.001	0.882(0.592,1.313)	0.536
NO	1.439(1.038,1.997)	0.029	1.466(1.002,2.146)	0.049
Higher age at menarche	0.985(0.929,1.045)	0.627		NS
Gravidity	1.022(0.944,1.106)	0.596		NS
Parity	0.950(0.775,1.163)	0.618		NS

**Notes:** Estimates adjusted by menopause or not, age, level of education, soya products, daily exercise intensity, daily exercise amount, smoking, alcohol consumption, HRT, higher age at menarche, gravidity and parity. Data are reported as coefficient of regression (CR) and standard error (SE). NS, not significant. \* $P < 0.05$  is considered statistically significant.

education was positively associated with decreased odds of menopausal symptoms. Current smoking, gravidity and parity showed no relationship, but we found that increased alcohol consumption could aggravate VMS.

## Discussion

This is the largest cross-sectional study in Chinese women coming from all over China to one specialized center to evaluate menopausal symptoms and their variability with age and menopausal status, and to comprehensively assess their relationship with various social and environmental factors which could have an effect on menopausal complaints. Possible associations were assessed after rigorous multiple adjustments of all analyzed factors.

## Prevalence of Menopausal Symptoms and Dependency on Menopausal Status

All symptoms, except cognitive and urogenital symptoms, worsened age-dependently up to 60 years, but improved beyond this age and most, but not all, were also dependent on menopausal status, ie, with different risk in women who had experienced menopause. Regarding the time of menopausal transition, a meta-analysis of 36 studies evaluating age at natural menopause reported an overall mean of 48.8 years, with a range of 46 to 52 years.<sup>11</sup> Menopausal symptoms usually begin four to six years before cessation of menses.<sup>12</sup>

One of the main results of our study is that urogenital symptoms had the highest prevalence (97.9%) (Figure 1). The lowest prevalence was found for VMS (48.8%). This is in sharp contrast to the literature concerning menopausal

women in most Western countries, where up to 75% present with VMS as the main complaints.<sup>13</sup> Similar to reports from Western countries, the prevalence of negative mood in midlife women was also very high in our study (at 80.3%) and was the third most common symptom after urogenital complaints and limb pain/paresthesia (84.9%), beginning during menopausal transition and persisting beyond 60 years of age.

An increased risk of negative psychological symptoms during menopausal transition, such as anxiety and emotional distress, has been observed in many studies such as SWAN<sup>14</sup> and the Seattle Midlife Women's Health Study.<sup>15</sup> Furthermore, about 30% of women in SWAN experienced a worsening of depressive mood.<sup>14</sup> The risk of depressive symptoms and impairment of cognitive performance were significantly higher in women during the menopausal transition, with a lower risk after the final menstrual period (FMP).<sup>16</sup> However, in our previous study, we found that the prevalence and severity of depression was significantly higher in postmenopausal compared to perimenopausal women,<sup>17</sup> so there may be differences between study populations.

The SWAN study reported cognitive performance impairment during the menopausal transition, with subsequent improvement to premenopausal levels in the postmenopausal period.<sup>18</sup> However, in our study, decreased cognitive performance began during menopausal transition, lasted up to the age of 60 and then worsened during the following years.

Sleep difficulties often begin during menopausal transition, and the prevalence increases in post-menopausal

life (31% vs 40%-56%).<sup>19</sup> This is in line with our previous study, where we found that the prevalence and severity of insomnia was significantly higher in postmenopausal compared to perimenopausal women.<sup>17</sup> In the present study, complaints about insomnia also started in the menopausal transition and increased after menopause to a prevalence of 65.4%.

One study revealed that VMS can begin as early as two years before the FMP, peaks one year after the FMP and tapers off within a median time of 7.4 years in approximately half of women.<sup>20</sup> Approximately 12% of women will continue reporting symptoms as long as 11–12 years after the FMP.<sup>21</sup> In our study, VMS started during the menopausal transition and persisted even beyond the age of 60.

Women exhibit a decrease in sexual desire and an increase in painful intercourse beginning in the late perimenopause.<sup>22</sup> It was found that sexual dysfunction showed a steep decline in women 46 to 48 years of age, partly increased in the 49 to 51 years age group and declined at age 52 to 55 years.<sup>23</sup> In our previous study, we found that the prevalence and severity of sexual dysfunction was significantly higher in postmenopausal compared with perimenopausal women.<sup>17</sup> In our present study, we did not differentiate between urogenital symptoms and sexual dysfunction, ie, both symptoms were collected within the same group. We found that urogenital symptoms started during menopausal transition, increased in the 50–55 years age group, and further worsened after 60 years of age. To obtain more insight regarding the prevalence of sexual function would require more sophisticated evaluations, such as the use of special validated scores.

Women in different stages of reproductive life may have altered autonomic nervous system (ANS) function due to the different hormonal environment.<sup>24</sup> The ANS plays a key role in all cardiac regulatory mechanisms, exerting a tonic and reflexive influence on the main variables of the cardiovascular system, and an imbalance in ANS functioning leads to disease and mortality.<sup>25</sup> Estradiol is cardio-protective, associated with higher vagal activity and lower sympathetic nervous system (SNS) activity.<sup>26</sup> Progesterone is associated with higher SNS activity.<sup>27</sup> Therefore, not only dependency on age (Figure 2), but also dependency on the menopausal status should be expected, which, however, was not the result in our study (Table 2). However, in general, data on the issue of ANS are very rare and need more research. To our

knowledge, our results are the first to be published using a large population.

## Social and Environmental Factors Influencing Menopausal Symptoms

Regarding the possible etiology of menopausal symptoms, hormonal changes are well known to be responsible for these symptoms in type and severity,<sup>17</sup> as also published by our group elsewhere.<sup>17</sup> However, little is known about the relationship between menopausal symptoms and socio-demographic data, lifestyle, and dietary changes. Since BMI has been found to be positively related to the intensity of menopausal symptoms,<sup>12</sup> lifestyle and dietary changes may elicit indirect negative effects. Our study did have a relatively low BMI (24) in contrast to most Western studies, so the results of our study may not be extrapolated to other studies. Indeed, this should be also an argument, that it is necessary to perform studies especially for Chinese women, despite similar studies may already exist in Western world. There is increasing evidence that socio-demographic and environmental factors including childhood nutrition, disease exposure, energy expenditure, parity and smoking habits may exert a tremendous influence on menopausal symptoms.<sup>9</sup> The menopausal symptoms which we investigated in our study regarding possible associations are listed in Table 2, in terms of the different influencing factors and “crude” and adjusted *OR* values.

From our results it is notable that women with a higher level of education are less likely to have menopausal symptoms, in line with previous studies.<sup>28</sup> Level of education is suggested as being a good indicator of socioeconomic status and may affect menopausal symptoms by physiological effects on lifestyle behavior and reproductive health.<sup>29</sup> However, it may also be that women with higher education simply better cope with their VMS, for example by avoiding drinking too much coffee and alcoholic beverages and using suitable clothing.

Regular exercise can mitigate some menopausal symptoms and improve sleep quality.<sup>30</sup> In our study, we found protective effects on negative mood, insomnia, and autonomic nervous disorders, but no significant association with VMS, cognitive symptoms and limb pain/paresthesia. There may be some explanations for these negative results: Regarding VMS, it was demonstrated that increased physical activity leading to increased sweating and higher body temperatures is associated with higher rates of

VMS.<sup>3</sup> Regarding cognitive performance, it was hypothesized that there may be neuroprotection mediated through brain-derived neurotrophic factors and reduction of pro-inflammatory cytokines,<sup>31</sup> or reduction in cardiovascular risk through exercise may have a general health benefit.<sup>32</sup> However, in a randomized controlled trial, the effect of physical exercise on cognition was largely negative,<sup>33</sup> consistent with our results. Regarding limb pain/paresthesia, high-intensity exercise can induce collagen growth, but may also cause injuries to tendons and other soft tissue.<sup>34</sup>

Despite these negative results in our study and in other studies, adequate physical activity should be recommended also for menopausal women since it undoubtedly has many beneficial effects, not only for decreasing some of the menopausal symptoms, but particularly for postural stability, prevention of cardiovascular and bone disease.

Hormone replacement therapy (HRT) is well known to be the most effective way of relieving menopausal symptoms and preventing or reducing the occurrence of various chronic diseases.<sup>35,36</sup> However, because of risks such as breast cancer and thromboembolic diseases, patients and many doctors dislike using HRT or do not use HRT on a regular basis. Our study showed a decrease in all menopausal symptoms with HRT, which also clearly confirms that if there is a decision for HRT, it should be used at least for six months every day (Table 2) to achieve the benefits of estrogen replacement.

For patients with contraindications for HRT or who refuse hormonal therapy, there is broad consensus that soya products (eg, isoflavones in tablets) can be used because they contain phytoestrogens.<sup>37</sup> However, our study shows that if using a soya-rich diet, daily consumption is necessary to improve symptoms. Consumption only 2–3 times/week was mostly not effective (Table 2). To our knowledge, this was shown here for the first time in a large population study. To explain the different results of studies from Western countries, it must be considered that the amount of isoflavones in the normal Chinese diet (about 200 mg/day) is much higher than in “food supplements” offered in pharmacies (50 mg/day).<sup>37</sup>

It should be mentioned that we use instead of HRT also tibolone particularly in women with sexual complaints or negative mood, because of the well-known additional androgenic effects due to the progestational metabolite and because SHBG is decreased. Besides soy, we use alternatives for the treatment of VMS like hot flashes, especially if HRT is contraindicated, with good experience

using black cohosh for example in patients with breast cancer history. About this, we have published elsewhere.<sup>38</sup>

Regarding a possible association between menopausal symptoms and other related factors, which were investigated in our study, we found that current smoking, gravidity, parity, and menarche are not related to menopausal symptoms. We only found that alcohol consumption ( $\geq 3$  times/week) could aggravate VMS. This is in line with the results of Freeman et al, who found a significant positive association between alcohol intake and hot flashes.<sup>38</sup> However, the results in the SWAN study did not detect any effects of alcohol consumption on VMS.<sup>39</sup>

This and other differences can be explained as we performed simple and unconditional logistic regression methods with rigorous adjustment of all analyzed factors, with the consequence that we obtained similar results to other studies for some of those single factors in the “Crude OR”, ie, significant relationships, but not after multiple adjustments.

## Conclusion

All symptoms, except cognitive and urogenital symptoms, worsened age-dependently up to 60 years, but improved beyond this age, the strongest effect being the prevalence and severity of urogenital complaints. The prevalence of most menopausal symptoms, except negative mood and autonomic nervous disorders, is also dependent on the menopausal status, ie, increasing in postmenopausal compared to perimenopausal patients. Complex relationships with social/environmental factors may explain the fact that after rigorous adjustments, we only found an association between a higher level of education and less menopausal symptoms, and increase in VMS in women with increased alcohol consumption, but no relationship with age at menarche, gravidity, parity and smoking. Regular exercise was beneficial only for some of the symptoms, but it is recommended for maintaining general health. As expected, HRT can decrease frequency and severity of all complaints investigated in our study, but must be used regularly. Nutritional soya products are an effective alternative, but only with daily consumption. We should pay more attention to diet and lifestyle, as this may contribute to the control of menopausal symptoms.

## Strengths and Limitations

To our knowledge, this is the largest cross-sectional study on menopausal symptoms and associated social and

environmental factors in midlife Chinese women. Because the women came from 31 provinces, the results should be credible throughout China. It also is a strength that all women were patients from one center where data were collected and all clinical examinations were performed, and that this center is specialized in the field of menopause, being the first “Menopause Clinic Center” in China to be officially acknowledged by the health authorities.

Limitations are that there may be selection bias suggesting that more women with symptoms would come to our hospital and participate in this study. Another limitation is that our results are based on the baseline data of a prospective cohort study, more robust results need long-term follow-up. Another limitation is related to the very large number of women with urogenital symptoms, leading to a lack of control for analyzing multiple regression risk factors with urogenital symptoms.

## Data Sharing Statement

Because this cohort study is ongoing, the data is not available for readers.

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## Author Contributions

All authors made substantial contributions to conception and design, acquisition of data, or analysis and interpretation of data; took part in drafting the article or revising it critically for important intellectual content; agreed to submit to the current journal; gave final approval of the version to be published; and agree to be accountable for all aspects of the work.

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## Disclosure

The authors report no conflicts of interest for this work and declare that there are no conflicts of interest regarding the publication of this paper.

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