REVIEW

Revisiting the Duration of Vasomotor Symptoms of Menopause: A Meta-Analysis

Mary C. Politi, Ph.D.¹, Mark D. Schleinitz, M.D., M.S.², and Nananda F. Col, M.D., M.P.P., M.P.H., F.A.C.P.³

¹Department of Behavioral and Preventive Medicine, Brown Medical School, Providence, RI, USA; ²Department of General Internal Medicine, Brown Medical School, Providence, RI, USA; ³Center for Outcomes Research and Evaluation, Maine Medical Center, Portland, ME, USA.

BACKGROUND: Treatment decisions about menopause are predicated on a transient duration of vasomotor symptoms. However, evidence supporting a specific duration is weak.

OBJECTIVE: To estimate the natural progression of vasomotor symptoms during the menopause transition by systematically compiling available evidence using meta-analytic techniques.

DATA SOURCES: We searched MEDLINE, hand searched secondary references in relevant studies, book chapters, and review papers, and contacted investigators about relevant published research.

REVIEW METHODS: English language, population-based studies reporting vasomotor symptom prevalence among women in menopausal transition in time intervals based on years to or from final menstrual period were included. Two reviewers independently assessed eligibility and quality of studies and extracted data for vasomotor symptom prevalence.

RESULTS: The analyses included 10 studies (2 longitudinal, 8 cross sectional) with 35,445 participants. The percentage of women experiencing symptoms increased sharply in the 2 years before final menstrual period, peaked 1 year after final menstrual period, and did not return to premenopausal levels until about 8 years after final menstrual period. Nearly 50% of all women reported vasomotor symptoms 4 years after final menstrual period, and 10% of all women reported symptoms as far as 12 years after final menstrual period. When data were examined according to symptom severity ('any' vs. 'bothersome'), bothersome symptoms peaked about 1 year earlier and declined more rapidly than symptoms of any severity level.

CONCLUSIONS: Our findings suggest a median symptom duration of about 4 years among symptomatic women. A longer symptom duration may affect treatment decisions and clinical guidelines. Further prospective, longitudinal studies of menopausal symptoms should be conducted to confirm these results.

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BACKGROUND

As many as 15 to 30 percent of women consult physicians annually during the menopause transition^{1,2}, typically for symptom relief from vasomotor symptoms (i.e., hot flashes and night sweats)². Although some medical education materials and clinical guidelines³⁻⁵ report that most women experience vasomotor symptoms for 6 months to 2 years, many research findings report the duration as 4 years or more^{1,6}. Treatment decisions for menopausal symptoms are based on the transitory nature of these symptoms⁷.

The most effective treatment for vasomotor symptoms, menopausal hormone therapy (HT), has a risk:benefit profile that changes according to the duration and timing of treatment⁸. The risks and benefits of HT depend on duration of exposure to HT, and a woman's risk for incurring side effects and benefits associated with HT change as she ages. Some risks (i.e., stroke) are only apparent after 1-2 years of treatment, while others [venous thrombotic events (VTE)] appear much sooner⁹. Some risks (e.g., breast cancer) increase with longer duration of treatment¹⁰, while others (VTE and possibly coronary artery disease) appear to decrease over time.

Most clinical guidelines recommend using the lowest dose of HT for the shortest possible amount of time, based on assumptions about symptom duration and the known benefits of HT^{11,12}. Clinicians have advised women to attempt to discontinue HT every 6-12 months to determine if menopausal symptoms persist, as using HT for 1-2 years carries fewer risks than longer-term treatment. Guidelines assert that short-term treatment should be adequate to control symptoms during the menopause transition^{11,13}. However, symptoms may last longer than previously expected. A recent NIH consensus statement noted that there are limited data describing the duration of menopausal symptoms because studies do not often follow women beyond the first 2 years of postmenopause^{14,15}. Because the expected duration of symptoms is a critical factor in determining whether a woman decides to take HT, better evidence about symptom duration is needed.

Although some suggest that vasomotor symptoms may last longer than 1-2 years for a minority of women⁵, the average duration of symptoms and predictors of the length of symptoms are poorly described. Measuring the duration and natural progression of menopausal symptoms is challenging because of the variable symptoms included and attributed to menopause, the lack of standard definitions of symptoms, differences in recording symptom severity, the need to adjust for the use of any treatments that may relieve symptoms, the self-selection of women according to symptom severity, and recall error. Moreover, the information available is based on studies where the

symptoms were artificially truncated at the onset or the end of observation periods; symptoms may have begun before the study began and may have extended beyond the length of the study.

The studies that are frequently referenced (e.g.,^{16,17}) as establishing the duration of menopausal symptoms were not specifically designed to measure the length of time between the onset and cessation of menopausal symptoms. The definition and measurement of vasomotor symptoms, and the populations surveyed, varied considerably across these studies¹³. One of the most often cited studies reporting primary data about menopausal symptom duration¹⁶ relied on symptom recall 5 or more years after a woman's final menstrual period (FMP) and did not report any numerical data on symptom prevalence. Another frequently cited study¹⁷ did not report symptom duration, but instead reported the percent of women who experienced hot flashes in various time intervals after menopause: 1–2 years (35%), 3–5 years (28.6%), 6–10 years (26.2%), and 11+ years (10.3%). Thus, the majority (65%) of women in this study experienced hot flashes that lasted longer than 2 years, and 10.3% were still reporting hot flashes at the conclusion of the study. However, later references to this study^{6,18} commonly misinterpreted the data and stated that the majority of women experienced hot flashes for 1–2 years. In addition, neither of the aforementioned studies accounted for the use of HT or the potential truncation of symptoms at the beginning or end of the study. Many longitudinal and cross-sectional studies have subsequently been published that can potentially provide more robust data that can be used to address symptom duration.

The purpose of this study was to estimate the natural progression of vasomotor symptoms during the menopause transition by systematically compiling available evidence using meta-analytic techniques.

METHODS

Search Strategy. We performed a comprehensive Medline literature review in November 2007 to retrieve all English language studies that contained information on vasomotor symptom prevalence during the menopause transition. MeSH terms included: vasomotor.mp. or exp vasomotor system/(hot flash\$ or hot flush\$ or night sweat\$.mp. body temperature regulation/or sweating/combined with menopause/ OR climacteric/. We also searched the bibliography of relevant articles, relevant clinical manuals^{14,19}, chapters in text books, and review papers. We contacted authors of relevant papers for additional information on their data as needed.

Study Selection. To minimize selection and sampling bias, we excluded studies that were clinic-based and those that were randomized trials of menopausal treatment. We included both longitudinal and cross-sectional studies. If two or more studies described the same cohort, the single paper that presented the most complete data was selected. Data were extracted and independently rated by two readers (NC and MP). Final inclusion was decided by consensus. We rated the quality of studies using the Newcastle Ottawa Quality Assessment Scale for nonrandomized studies in meta analyses²⁰.

We defined vasomotor symptoms as any of the following: hot flushes, hot flashes, night sweats, and cold sweats. We did not

attempt to disaggregate specific vasomotor symptoms because few studies reported outcomes separately for isolated symptoms. To account for differences in the severity of vasomotor symptoms reported, we distinguished between two groups of studies: those reporting any level of symptom, regardless of severity (reported as “any symptom”), and those reporting bothersome, or moderate to severe symptoms (reported as “bothersome symptoms”).

To compare prevalence rates at various points in time across studies that reported vasomotor symptoms according to years to or from FMP^{2,21–25}, we defined the FMP as our index time point. The number of years to or from FMP comprised the time scale.

Four studies^{26–29} did not report symptoms according to years to or from FMP, but according to menopausal stage. We used criteria developed by the Stages of Reproductive Aging Workshop (STRAW) (30) to standardize the definitions of menopausal stages: premenopause (regular menstrual cycles): S₋₃; early perimenopause (variable cycle length of >7 days different from normal): S₋₂; late perimenopause (variable cycle length of ≥2 skipped menstrual cycles and an interval of amenorrhea ≥60 days): S₋₁; early post-menopause (within 4 years of FMP): S₁; late post-menopause (>4 years from FMP): S₂. In two of these studies^{26,29} we only included data through perimenopause because the definitions for post-menopause were too broad (e.g., anytime >12 months since FMP).

We excluded studies^{31–34} that reported menopausal symptoms using rating scales (e.g., Greene Climacteric Scale) because the scales measured symptom severity rather than symptom prevalence. Additionally, these scales used different units of measurement that could not be directly compared.

Analysis. We pooled vasomotor symptom prevalence from each study at various time intervals in the menopausal transition using MOOSE guidelines for meta-analysis³⁵. Our primary analyses were based on years to or from FMP, which allowed us to determine changes in symptom prevalence in 1-year intervals. Secondary analyses were based on menopausal stage according to STRAW criteria. We used Meta-Analyst³⁶ to pool data based on the random effects model of DerSimonian and Laird³⁷. We assessed for heterogeneity by calculating the *Q*-statistic for each independent time point and found none.

The main analyses included studies that reported symptoms of any level of severity. Some studies also included prevalence points for ‘bothersome’ or ‘moderate to severe’ symptoms. We stratified analyses according to level of symptoms reported (‘any’ versus ‘bothersome’ symptoms) and graphed the pooled symptom prevalence at each point in time. We were not able to stratify results by study design (e.g., longitudinal vs. cross-sectional) or exclusion/inclusion of HT users because there were too few studies in each category.

Role of the Funding Source. The AHRQ funded this study, but did not participate in data extraction, analysis, or interpretation of the data, synthesizing of the conclusions, or preparation of the manuscript.

RESULTS

Study Characteristics. A total of 410 studies were initially identified by our search strategy; data were formally extracted from 63 studies. Ten studies^{2,21–29} met inclusion criteria and

Figure 1. Study flow diagram.

were included in the meta-analysis (Fig. 1). Of these, six^{2,21-25} reported vasomotor symptoms by years to or from FMP, and four²⁶⁻²⁹ reported symptoms based on STRAW stages. Three^{2,26,27} were longitudinal, 7^{21-25,28,29} were cross-sectional. One longitudinal study also included a cross-sectional survey²⁶; only the cross-sectional survey was used in the meta-analysis because it provided more complete data on symptom prevalence according to menopausal stage.

The studies included a total of 35,445 participants whose age ranged from 39–65 at study inception and up to age 75 at the end of study follow-up (Table 1). Only one study²⁶ reported the ethnic or racial background of participants. Seven studies described the time interval for symptom reporting: four^{2,26,28,29} reported symptoms during the past 2 weeks, two^{21,27} reported vasomotor symptoms during the past year, and one²² reported symptoms in the previous month. Three^{2,22,26} reported symptoms based on level of severity. Based on the Newcastle-Ottawa Quality Assessment Scale²⁰, all studies scored highly on sample representativeness, and both longitudinal studies scored highly on follow-up assessment (Appendix A). Few controlled for the use of HT, but

Figure 2. Vasomotor symptom prevalence by years to/from final menstrual period. Six studies^(2, 17-21) provided data for the main meta-analysis. One⁽²⁾ was longitudinal, and the others were cross-sectional. The onset of menopause (Y₀) coincides with the final menstrual period (FMP). One year after FMP corresponds to Y₁, two years after, Y₂, etc, whereas Y₋₁ represents 1 year before FMP.

almost all controlled for other biasing factors such as surgical menopause. All assessed vasomotor symptoms by self-report.

Vasomotor Symptom Prevalence. The six individual studies that assessed vasomotor symptom prevalence by years to or from FMP were remarkably consistent with each other in the rise and fall of symptom prevalence according to years from FMP (Fig. 2), with the exception of one study²¹ that reported erratic peaks and troughs until 6–7 years after FMP.

When all studies reporting vasomotor symptom prevalence according to years to or from FMP were combined, a temporal pattern emerged. The percentage of women experiencing symptoms began to increase in the years before menopause, peaked at approximately 1 year after FMP, and did not return to premenopausal levels until about 8 years after FMP (Fig. 3). Symptom prevalence fell to half of its peak prevalence only at 6.5 years after

Table 1. Characteristics of Studies Included in Meta-analysis

	Year	Country	N at Inception	Age at Study Start	Time Line Used ^a	Included HT Users?	Assessed Symptom Severity?
Thompson²³	1973	UK	269	40–60	Years to/from FMP	Y	N
McKinlay^{21b}	1974	UK	638	45–54	Years to/from FMP	Y	N
Berg^{24c}	1988	Sweden	1,469	60–62	Years to/from FMP	Y	Y
Oldenhave²²	1993	The Netherlands	5,213	39–60	Years to/from FMP	Y	Y
Nedstrand^{25d}	1996	Czech Republic	799	55–65	Years to/from FMP	Y (n = 1)	N
Guthrie²	2003	Australia	438	45–55	Years to/from FMP	Y	Y
Groeneveld²⁸	1996	The Netherlands	1,947	45–60	STRAW staging	Not reported	N
Brown²⁷	2002	Australia	8,466 ^e	45–50	STRAW staging	N	N
Avis⁵³	2005	US	16,065	40–55	STRAW staging	N	Y
Melby²⁹	2005	Japan	140	45–55	STRAW staging	N	N

^aFMP=final menstrual period; STRAW=Stages of Reproductive Aging Workshop

^bSeparated hot flashes and night sweats; data on hot flashes is presented because it was more complete (with percentages and duration)

^cCombines data from two studies of the same cohort

^dReported percentages only; to calculate a total N for each year to/from final menstrual period, we assumed an equal distribution of the total sample for each menopausal group

^eTotal N for our analyses based on e-mail correspondence with author and her statistician

Figure 3. Pooled estimates of proportion of vasomotor symptoms by years to/from final menstrual period. Six studies^(2,17–21) provided data for the main meta-analysis. One⁽²⁾ was longitudinal, and the others were cross-sectional.

FMP. At 2 years before FMP, the earliest year for which we had more than one study reporting symptom prevalence, vasomotor symptom prevalence was 13.9% (95% CI 9.8–19.3%). At its peak, 1 year after FMP, it was 55.7% (95% CI 50.1–61.3%), dropping to 28.9% (95% CI 21.6–37.4%) at 5 years after FMP. Symptom prevalence returned to baseline rates 8 years post FMP. Confidence intervals were broad beyond 5 years post FMP due to small sample sizes.

When data were stratified according to symptom severity ('any' vs. 'bothersome'; Fig. 4), bothersome symptoms peaked around 1–2 years after FMP, whereas the prevalence of any symptom peaked 2–3 years after FMP. Furthermore, while bothersome symptoms sharply declined 3–7 years after FMP, the presence of any symptom declined at a much slower rate.

Secondary Analyses Using STRAW Criteria. Similar patterns emerged when data were pooled according to STRAW menopausal stage. Vasomotor symptom prevalence at premenopause (STRAW

stage S₋₃) was 15.6% (95% CI 12.0–19.9%), similar to the premenopausal rate based on years to or from FMP. Vasomotor symptom prevalence peaked during early post-menopause (defined as up to 4 years after FMP), with a prevalence of 59.8% (95% CI 56.6–63.0%). However, prevalence rates never returned to baseline, with 43.9% (95% CI 34.2–54.1%) still reporting symptoms at late post-menopause, defined as more than 5 years after FMP (STRAW stage S₂).

Analysis of Excluded Studies. To explore for the presence of bias resulting from our inclusion criteria or definitions, we conducted separate analyses of the ten studies that were excluded^{1,38–46} because they reported symptom prevalence at time points that could not be mapped to either years to or from FMP or STRAW criteria (Appendix B). A scatter plot of these studies showed a trend consistent with those in the meta-analysis, although the exact timeline could not be determined. Vasomotor symptom prevalence peaked around menopause, declined post menopause, but never returned to premenopausal rates.

DISCUSSION

This creative method of sequentially pooling prevalence across studies provides comprehensive time series data that can accurately portray the natural history of vasomotor symptoms during the menopause transition. Among the women experiencing vasomotor symptoms, our data show a peak vasomotor symptom prevalence at 1 year after FMP, with 50% of women reporting symptoms after 4 years and 10% reporting symptoms as far as 12 years after FMP.

Our findings are consistent with other recent cohort studies that explored symptom prevalence. In one study of older postmenopausal women (mean age, 67 years), over 30% of women experienced vasomotor symptoms more than 3 years after FMP⁴⁷. Another longitudinal study suggested that women began experiencing vasomotor symptoms approximately 2 years before FMP and that symptoms tended to last for a median of

Figure 4. Meta-analysis stratified by symptom severity. Six studies^(2,17–21) provided data for the main meta-analysis. One⁽²⁾ was longitudinal, and the others were cross-sectional. The fitted trendlines (Fig. 4) were created to represent the pattern of vasomotor symptom prevalence over time, using a third order polynomial function.

4 years². In that cohort, as many as 20% of women reported hot flashes for more than 5 years⁴⁸.

If the duration of vasomotor symptoms is approximately 4 years, as our findings suggest, the clinical implications are substantial. A longer symptom duration may affect treatment decisions and clinical guidelines. The risks of diseases that are either induced or averted by HT, as well as the continuation of symptoms that can impact women's quality of life with premature discontinuation of HT⁴⁹, need to be carefully weighed in determining an individual's risk:benefit profile from HT or non-hormonal treatments.

There are also implications for research examining vasomotor symptom duration. The studies that laid the foundation for the duration of vasomotor symptoms were not designed to measure symptom duration. Methodologically robust prospective, longitudinal studies that examine symptom duration are needed to better understand the natural history of menopause. Ideally, studies should begin observation before the onset of symptoms, continue until symptoms cease, and account for level of symptom severity and the use of symptom-modifying treatments. Prospective data acquisition is needed to minimize recall error. Moreover, research should also aim to identify risk factors for persistent vasomotor symptoms among menopausal women. Only one longitudinal, epidemiological study to date has investigated risk factors such as socioeconomic status, lifestyle behaviors, and physical and psychological health on the presence of vasomotor symptoms^{26,50,51}, and found that menopausal status was the most consistent predictor of the presence of symptoms.

Although the STRAW criteria have helped to standardize nomenclature around the menopause transition, its broad categorization of time intervals, especially for late postmenopause, makes it less useful in determining the duration of symptoms. Further refinement of later postmenopause, using smaller incremental time intervals, would help characterize the duration of menopausal symptoms.

Limitations. Our findings should be interpreted with caution because of the difficulties in translating symptom prevalence data into estimates of symptom duration. Symptom prevalence data do not allow us to determine when individual women started experiencing symptoms or when their symptoms abated. Simulation techniques could be used to estimate duration from prevalence data, but such analyses are beyond the scope of the present paper.

Additionally, many of the studies were cross-sectional and may have been subject to sampling variability. Although we excluded studies that were clinic-based to minimize the selection of more symptomatic women (selection bias), longitudinal studies with longer periods of follow-up would provide better estimates of the time course for symptom onset, prevalence, and severity of vasomotor symptoms over time.

Our estimates should be interpreted cautiously because the studies included in our analyses artificially truncated symptoms due to limited follow-up periods; that is, symptoms may have begun before the study began and may have extended beyond the length of the study.

Differences in the minimum level of symptom severity among studies could result in an underestimation of symptom prevalence. However, while studies reporting only women who had moderate, severe, or bothersome symptoms had lower symptom prevalence rates than studies that reported women experiencing

any level of symptom severity, the patterns observed were similar across all groups.

Some studies excluded women who were taking HT, which could introduce a selection bias that would underestimate both the duration and severity of symptoms, as HT users likely had more severe baseline symptoms and obtained symptom relief while on HT. We were not able to stratify our analyses according to HT use because there were not enough studies excluding HT users.

Differing selection and retention rates in the studies included in our analysis could have affected our results. Those who participated or remained in a study for longer periods of time might have experienced more severe or longer duration of symptoms. Nonetheless, temporal patterns observed across diverse studies were remarkably consistent, suggesting that this selection and retention bias was either consistent across all studies or relatively insignificant.

Although our analyses included studies conducted in multiple countries, it may not be generalizable to non-white women. Only one study²⁶ in our analyses included ethnically diverse participants. There is some evidence to show that vasomotor symptom reporting differs across ethnic groups⁵². However, to our knowledge, there is no evidence to show that vasomotor symptom duration differs by ethnicity.

In conclusion, these results suggest that the vasomotor symptoms of menopause may last longer than 2 years, and for a median of about 4 years. The data should lead to reevaluating the course of treatment of menopausal symptoms given the risks and benefits of longer-term use of HT. Further prospective, longitudinal studies of menopausal symptoms that account for the presence of symptoms before and after the observation period, the use of symptom-modulating treatments, such as HT, symptom severity, and ethnicity should be conducted to confirm these results. Studies should also assess potential risk factors for persistent vasomotor symptoms and typical age of onset of these symptoms.

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Corresponding Author: Mary C. Politi, Ph.D.; Department of Behavioral and Preventive Medicine, Brown Medical School, CORO Suite 500, 1 Hoppin St, Providence, RI 02903, USA (e-mail: mary_politi@brown.edu).

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APPENDIX A

Quality assessment based on the Newcastle-Ottawa Quality Assessment Scale

Table 2.

	Year	Represent-ative cohorta	Symptoms Present at inceptionb	Comparable (controls for HT, or other bias)c	Assessment of outcomed	F/U lengthe	Adequacy of F/Uf
Thompson ²³	1973	Truly*	N/A	Surgical menopause*	Self-report	N/A	N/A
McKinlay ²¹	1974	Somewhat*	N/A	Surgical menopause*	Self-report	N/A	N/A
Berg ²⁴	1988	Somewhat*	N/A	Reported but not controlled	Self-report	N/A	N/A
Oldenhave ²²	1993	Somewhat*	N/A	Surgical menopause, contraceptives*	Self-report	N/A	N/A
Nedstrand ²⁵	1996	Somewhat*	N/A	Reported but not controlled	Self-report	N/A	N/A
Guthrie ²	2003	Truly*	Controlled*	HT, surgical menopause**	Self-report	8 years*	88*
Groeneveld ²⁸	1996	Truly*	N/A	HT, surgical menopause**	Self-report	N/A	N/A
Brown ²⁷	2002	Somewhat*	Controlled*	Surgical menopause*	Self-report	2 yrs*	92*
Avis ⁵³	2005	Truly*	N/A	HT, Surgical menopause**	Self-report	N/A	N/A
Melby ²⁹	2005	Truly*	N/A	HT, Surgical menopause, contraceptives**	Self-report	N/A	N/A

^aTruly representative or somewhat representative=* rating

^bOutcome of interest not present at start of study=* rating

^cControls for HT=* rating; controls for HT AND other bias (e.g., excluding women who experienced surgical menopause)=** rating

^dIndependent blind assessment or record linkage=* rating

^eLong enough follow-up for outcomes to occur=* rating

^fAdequacy of follow-up rate=* rating

APPENDIX B

Characteristics of studies with vague menopausal staging criteria

Table 3.

	Year	N at inception	Years of follow-up	Starting age (years)	Definition of menopausal phases*	Measurement of vasomotor symptoms
Kaufert	1981	148	N/A	mean 50	Pre, peri/immediately post, advanced post	% with symptoms
McKinlay	1992	2,570	5	44–55	Pre, peri, T0, post	% with symptoms in past 2 weeks
Hunter	1992	36	3	47+	Pre, peri/post	% with symptoms
Bardel	2002	2,991	N/A	35–64	Pre, men, post	% with symptoms
Overlie	2002	57	5	47–55	Pre, <1 year post, 1–4 years post	% with symptoms
Keenan	2003	2,602	N/A	45+	Menstruating vs. not	% with symptoms
Juang	2005	1,273	N/A	40–54	Pre, peri, post	% with symptoms in past 2 weeks
Kumari	2005	2,489	N/A		Pre, peri, post	% with symptoms
Miller	2006	356	N/A	45–54	Pre, peri	% with symptoms
Sievert	2006	293	N/A	45–55	Pre, peri, post	% with symptoms

*Pre=premenopausal; peri=perimenopausal; T0=final menstrual period; men=menopausal; post=postmenopausal