Maturitas, 14 (1992) 103–115
Elsevier Scientific Publishers Ireland Ltd.

MAT 00661

The normal menopause transition

Sonja M. McKinlay, Donald J. Brambilla and Jennifer G. Posner

New England Research Institute, 9 Galen Street, Watertown, Massachusetts (U.S.A.)

This paper presents analyses from perhaps the largest and most comprehensive prospective cohort study of mid-aged women — the Massachusetts Women's Health Study (MWHS) — with numbers sufficient to provide, for the first time, stable estimates of parameters in the normal menopause transition. The three questions addressed in this analysis are (i) what are the natural menopause transitions and when do they occur, (ii) what factors affect these transitions and (iii) what signs and/or symptoms accompany these transitions? The data were obtained primarily from 5 years of follow-up of 2570 women in Massachusetts who were aged 45–55 years as of January 1, 1982. An initial baseline cross-sectional survey (T_0) yielded a total of 8050 completed responses with an overall response rate of 77%. From this cross-sectional sample a cohort of approximately 2570 women was identified, consisting of women who had menstruated in the preceding 3 months and who had not undergone removal of the uterus and/or ovaries. Prospective study of the cohort consisted of six telephone contacts (T_1–T_6) at 9-month intervals with excellent retention of the respondents. A subset of the full cohort was defined that consisted of women who were premenopausal (rather than perimenopausal) at baseline (T_0) (n = 1178). Confirming prior reports, the age at natural menopause occurred at 51.3 years with a highly significant median difference (1.8 years) between current smokers and non-smokers. The new analyses reported here on median age at inception of perimenopause (47.5 years) and factors affecting it are consistent with findings for age at last menstrual period, particularly the overwhelming effect of smoking. Smokers tend to have not only an earlier but also a shorter perimenopause. The length of the perimenopausal transition (estimated at nearly 4 years) has not been previously reported. Moreover, the highest rate of physician consultations is observed among those with longer perimenopause transitions. The relationship between menopause transitions and symptom reporting appears to be transitory, with reported rates showing an increase in the perimenopause and a compensatory decrease in the postmenopause. The implications of combined hormone replacement therapy for future research on menopause in industrial societies is discussed in relation to these findings.

Key words: menopause; longitudinal study; median age; symptoms

Introduction

In the United States, as in other western countries, women now live an average of 75–80 years [1]. Mortality from childbirth is now negligible and death rates before the age of 50 from all other causes are very low [1]. The implication is that the overwhelming majority of women in advanced societies experience menopause — cessation of menses — and can expect to live approximately 30 years beyond this event.

Correspondence to: S.M. McKinlay, New England Research Institute, 9 Galen Street, Watertown, MA 02172, U.S.A.

0378-5122/92/$05.00
Printed and Published in Ireland

Indeed, the expected adult life span beyond this natural event is now nearly equivalent to the reproductive life span before it.

Despite the ubiquity of menopause in western societies, very little is known concerning the normal range of experience of this event and the factors which may affect it. Almost all of the population-based research concerning this event has been cross-sectional or retrospective. A comprehensive review, published nearly two decades ago by McKinlay and McKinlay [2], provided a critique of all of the literature on the menopause to that date and concluded that knowledge could only be advanced by conducting a prospective study to observe women as they approached and experienced this event. Cross-sectional designs can only identify associations (real or spurious). Longitudinal cohort designs can facilitate identification of those associations that are most likely to reflect a cause-effect relationship, through observation of temporal sequences in events or rate changes.

Since that review, the only prospective studies reported in the literature have been severely restricted, methodologically. Three important cohort studies of random samples of community populations, or the equivalent have been restricted in numbers [3–5]. Holte and Mikkelsen (1982) sampled and followed 200 urban women aged 45–55 [3]. Kaufert et al. (1984) followed 500 women aged 45–55 (of whom 369 had menstruated in the 3 months prior to the original survey and 131 had had a surgical menopause) identified in a larger cross-sectional sample of 2500 women aged 40–60 in Manitoba, Canada [4]. The study reported by Mattews et al. (1990) sampled 541 premenopausal women aged 42–50 years from driving licence lists in Allegheny Co., Pennsylvania (a relatively well-educated sample of white women [5]. Treloar (1974), reported menstrual histories on a sample of 324 women [6]. All were recruited as volunteers while they were students at the University of Minnesota. No data other than menstrual histories were collected on this cohort.

This paper presents analyses from perhaps the largest and most comprehensive prospective cohort study of mid-aged women — the Massachusetts Women's Health Study (MWHS) — with numbers sufficient to provide, for the first time, stable estimates of parameters in the normal menopause transition. The three questions addressed in this analysis are:

1. What are the natural menopause transitions and when do they occur?
2. What factors affect these transitions?
3. What signs and/or symptoms accompany these transitions?

Methods

Sample

The data for this paper were obtained primarily from 5 years of follow-up of 2570 women in Massachusetts who were aged 45–55 years as of January 1, 1982. The study began in late 1981 with a baseline cross-sectional survey (T_0) that employed a two-stage cluster sampling design. A total of 8050 completed responses were obtained from women randomly selected from annually compiled census lists. These responses were obtained by mailed questionnaires or telephone interviews of women who did not respond to mailings. The overall response rate was 77%.

From this cross-sectional sample a cohort of approximately 2570 women was identified, consisting of women who had menstruated in the preceding 3 months and who had not undergone removal of the uterus and/or ovaries. Prospective study of the cohort consisted of six telephone contacts (T_1–T_6) at 9-month intervals. Retention of the cohort was excellent, with response rates of 94–99% over the six contacts. At each contact an interview was conducted which included questions relating to current health status, health service utilization, menstrual status, employment and changes in selected sociodemographic characteristics.

A subset of the full cohort was defined that consisted of women who were premenopausal (rather than perimenopausal) at baseline (T_0) (n = 1178). The rather conservative definition employed in determining menstrual status is provided below.

The baseline sample, the full cohort and the premenopausal subcohort constitute the primary data sets for addressing the three questions posed above.

Measurement

All of the data, as indicated above, were self-reported, via mailed questionnaire or telephone interview. Data quality was high and consistent, as indicated by several methodological reports [7–11].

Two menopause events were defined. Natural menopause, or the natural cessation of menses, was defined retrospectively after 12 consecutive months of amenorrhea (spanning two contacts). This epidemiological definition is consistent with patterns noted by Treloar [6] and with definitions used in other large studies in Europe, North America and elsewhere [4,12,13,]. Women who had had a surgical menopause — cessation of menses resulting from removal of the uterus, with or without bilateral oopherectomy — were included only in selected analyses.

Three natural states were also defined, which together constitute the natural menopause transition. Women who had menstruation within the prior 3 months, with no change in regularity of cycle or a change that was reported at only isolated interviews were considered premenopausal. Women who reported 3–11 months of amenorrhea at one contact or increased menstrual irregularity at one, followed by more such irregularity or 3–11 months of amenorrhea at the next, were considered perimenopausal. This definition follows closely the perimenopausal menstrual patterns reported by Treloar [6] and compensates for any reporting ambiguities by using reports from two consecutive time points, rather than just one. The postmenopausal state consists of permanent amenorrhea, caused naturally or surgically.

Several factors potentially affecting aspects of the menopause transition were considered as covariates; these being age (in years, at last birthday), education ($<$ 12, 12, $>$12 years), parity, body mass index (kg/m^2) and current cigarette smoking. These factors have been variously implicated in variation in the age of natural menopause [8,13].

A list of signs/symptoms frequently cited as accompanying the menopause transition [2,14] were also considered and were imbedded in an expanded list of common complaints. Each subject was asked whether she had experienced in the preceding 2 weeks any of the following 22 signs/symptoms: hot flashes/flushes, cold sweats,

vertigo (dizzy spells), feeling blue or depressed, headaches, insomnia (trouble sleeping), palpitations (rapid heart beat), lack of energy, diarrhea and/or constipation, persistent cough, backaches, upset stomach, aches/stiffness in joints, shortness of breath, sore throat, loss of appetite, menstrual problems, fluid retention, difficulty in concentrating, nervous tension, urinary tract/bladder infections and "pins and needles" in hands or feet.

The analytic strategies were varied and complex, depending on the type of data set (cross-sectional or longitudinal) and are described in the context of the results themselves. Table I summarizes selected baseline characteristics for all three data sets used in the analyses.

The marked decrease in the percentage aged over 50 years reflects the removal from the cohorts of post- or perimenopausal women. The age distribution in the original survey was uniform (approximately the same number of women sampled for each year of age). The inverse trends in the percentage with > 12 years of education and the percentage of smokers mirror the strong relationship between smoking and educational level [13] as well as the strong effect of smoking on ovarian function (to be discussed below). The different percentages reporting hot flashes reflect different representations of menstrual states in the three data sets. Apart from these interrelationships, the data sets are equivalent with respect to marital and employment status. Hormone therapy shows low rates at baseline (1981–82). The higher rate in the baseline survey data set reflects the inclusion of 28% women who had had a surgical menopause. More than half of the HRT users in this data set were those who had had a surgical menopause. The 1% rate in the premenopausal subcohort includes women on combined therapy (who may have been perimenopausal at the time of first prescription). The percentage of all incident users (first reported use at T_1–T_6) in the full cohort was 13% (not shown in Table I). Only two-thirds of these ever users reported consistent use for two or more consecutive contacts. Of the 140 reporting a surgical menopause in the cohort, 87 (62%) began using hormones, most on a continuing basis. Because HRT was first prescribed predominantly in women defined

TABLE I

SELECTED CHARACTERISTICS OF THE PREMENOPAUSAL SUBCOHORT, COMPARED WITH THE ENTIRE COHORT AND WITH THE BASELINE (T_0) SURVEY SAMPLE

Characteristic (T_0)	Baseline survey sample (n = 8050)	Full cohort (T_0) (n = 2570)	Premenopausal subcohort (T_0) (n = 1178)
Percent age > 50 years	48.8	20.6	14.4
Percent > 12 years education	34.7	42.7	44.7
Percent married	74.5	76.8	75.7
Percent employed for pay	67.9	70.7	71.1
Percent current cigarette smokers	38.8	33.6	33.5
Percent HRT users	8.0	1.9	1.0
Percent hot flashes in 2 weeks	34.8	22.0	13.4

as peri- or postmenopausal, users were excluded from analyses involving perimenopause and the transition to postmenopause. Exclusion of HRT users for these analyses had no effect on the results as the numbers were small.

Results

Timing of the natural menopause transitions

The only natural transition which has been described in the literature is that to a natural postmenopause. The studies concerned have been thoroughly reviewed elsewhere [13]. When cross-sectional studies of Caucasian populations, which use appropriate logit (or probit) analyses of the age-specific proportions that have reached this transition are considered, the estimated median age at last menstrual period (LMP) lies between 50 and 52 years [13]. The equivalent estimate from the baseline survey sample is 51.3 years [13]. Taking account of the competing risk of surgical menopause does not alter these estimates [8,15].

An equivalent logit analysis was performed on the data set from the baseline survey to estimate the median age at inception of perimenopause, using the age-specific proportions that have reached perimenopause. The median, adjusted for actual age by adding 0.5 years to the estimate, was 47.5 years.

The trends in the age-specific prevalence of perimenopause are postmenopause are shown in Fig. 1, excluding women with a surgical menopause. The difference of 3.8 years between median age at peri- and postmenopause provides an estimate of the median length of the perimenopausal state. When the observed proportions reaching menopause after 1–5 contacts reporting perimenopausal signs are modelled in the premenopausal subcohort, a constant transition probability of 52% provides the best fit (Table II).

Nearly 10% of the premenopausal subcohort reached a natural menopause after only one contact reporting perimenopausal signs. From the definitions used in this paper, this means that nearly 10% ceased menstruating abruptly, with no prolonged irregularity (all reported at least 3 months of amenorrhea, including the most recent 3 months, in the 9 months since prior contact).

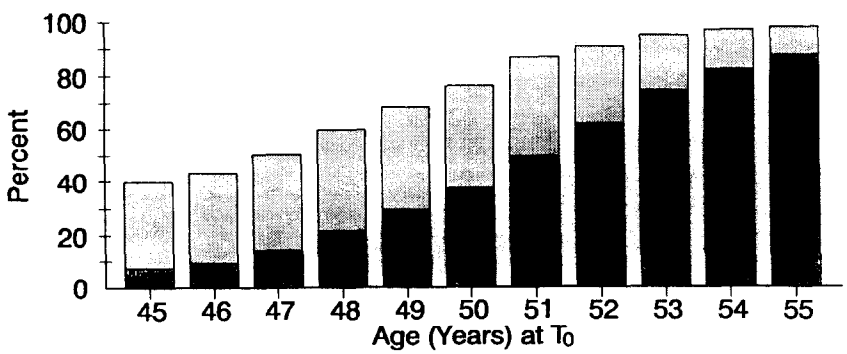

Fig. 1. Percentage distributions, by age, at T_0 for two menopausal transitions, excluding surgical menopause: MWHS 1981–82 (n = 5547). ■, Percent postmenopause; ▨, percent perimenopause. Median age at inception of perimenopause: 47.5 years, median age at menopause (LMP): 51.3 years.

TABLE II

OBSERVED AND ESTIMATED PROBABILITIES OF REACHING MENOPAUSE AFTER UP TO FIVE CONTACTS REPORTING PERIMENOPAUSE (n = 983*)

No. of contacts of perimenopause	Probability of reaching menopause at next contact	
	Observed	Expected**
1	0.09	0.09
2	0.21	0.22
3	0.39	0.38
4	0.57	0.58
5	0.68	0.78

*Excludes 195 women who did not reach perimenopause by T_5 (119), began using menopausal estrogens prior to perimenopause (43), or were censored after only one contact of perimenopause (33).

**Assuming a constant increase in transition probabilities of 52%.

Factors affecting menopause transition timing

Using the baseline survey data set, estimates of the median age at LMP were obtained for subgroups defined on categories of potential predictors. Of the four subgroups considered, education (<12, 12, >12), parity (0, 1+ children) and cigarette smoking (yes/no as well as number of packs per day), only current smoking (yes/no) provided significantly different estimates. The median for smokers was 50.2 years (± 0.05), while for non-smokers (including ex-smokers) it was 52.0 years (± 0.02) [13]. A small but non-significant dose-response effect was observed, declining as smoking increased.

Data from the full cohort were analyzed using a grouped survival model to investigate variation in age of natural menopause with the factors listed above, as well as use of oral contraceptives or HRT, income, marital status and urban/rural location [8]. Confirming the logit analysis of the cross-sectional data, current smoking status was the only statistically significant factor contributing to the timing of LMP ($P < 0.001$).

Using logistic regression in the premenopausal subcohort, factors associated with the transition to perimenopause were considered. A dichotomous dependent variable was created such that a code of 1 was assigned if a subject became perimenopausal by T_6, and a code of 0 was assigned otherwise (still premenopausal). Women who had had hysterectomies and/or bilateral oophorectomies prior to perimenopause were excluded. Five factors were considered: age at T_0, smoking (smoker/non-smoker at T_0), parity (0, 1+), education (<12, 12, >12 years) and BMI. The results are presented in Table III.

The best model included age, smoking and parity. Interactions between age and the other terms were considered but were not significant. As expected, older women and smokers were more likely to reach the perimenopause by T_6. The contribution of parity reflects early perimenopause among nulliparous women. These trends are summarized in Table IV.

The effects of the same five factors on the duration of the perimenopause were also

TABLE III

RESULTS OF LOGISTIC REGRESSION TO DETERMINE FACTORS AFFECTING THE PERIMENOPAUSE TRANSITION (n = 1138)

Best logistic model:		χ^2	P
Variable	Estimate		
Age	0.38	56.8	< 0.0001
Smoking	0.82	14.4	< 0.001
Parity	−0.13	6.3	0.012
Intercept	−16.51	—	—

examined using step-wise models. First, logistic regression was employed to determine whether the probability that a woman had only one perimenopausal contact varied with any of the five. The final model included only smoking and age at T_0. A smoking × age interaction was not statistically significant. Parameter estimates from the final model indicate that older women are more likely to have a shorter perimenopause (odds ratio for 5-year age difference: 2.34). Smokers are also more likely than non-smokers to have a shorter perimenopause (odds ratio: 1.84).

The analysis was then expanded to determine whether the actual number of perimenopausal contacts varied with age and smoking. This possibility was explored in a stepwise loglinear model that included smoking, the age at which the perimenopause started (two age groups) and the number of perimenopausal contacts that were reported (1–2, 3–4 or 5–6). A term for the first contact at which the perimenopause was reported was also included to control for the right censoring in the data. The final model included all six of the two-way interactions among these terms but no higher order interactions; thus, the effects of smoking and age on the duration of the perimenopause are again independent of each other. Examination

TABLE IV

SUMMARY OF ASSOCIATIONS WITH TRANSITION TO PERIMENOPAUSE (n = 1178)

Characteristic		Percent perimenopausal by T_6	Total (100%)
Age (T_0)	45 years	79	215
	46–47	87	393
	48–49	93	293
	50–55	97	271
Smoking (T_0)	No	87	775
	Yes	93	391
Parity	0	97	111
	1+	88	1064

of the parameter estimates indicates that smokers are more likely than non-smokers to have fewer perimenopausal contacts in pair-wise comparisons. The older women are also more likely to have 1–2 rather than 3–4, or 3–4 rather than 5–6 perimenopausal contacts. Thus, the impact of age and smoking on the duration of the perimenopause goes beyond simply predicting women who have the shortest perimenopause.

Signs/symptoms associated with menopause transitions

Reporting rates of three frequently cited symptoms, viz. hot flashes, cold sweats and insomnia, were considered in relation to the two transitions (to peri- and to natural postmenopause). Initial cross-tabulations indicated strong associations among the three, as expected from prior multivariate analyses [14,16–19]. Roughly half of those who reported hot flashes at each contact also reported cold sweats. Insomnia was more than twice as likely to be reported by women who experienced hot flashes than others. This probably reflects sleep disturbance from frequent flashes (and sweats) during the night [20].

Reports of hot flashes, sweats and insomnia were coded as one group of symptoms that is most likely to be related to one or both of the menopause transitions. Reports of the seventeen other symptoms about which women were questioned were grouped together into a second set. The frequency of these two groups of symptoms, separately and together, were considered by menopause status at T_6 (Fig. 2). This graph, which shows cross-sectional data, indicates that the perimenopausal increase in total symptom reporting is primarily due to an increase in the proportion of women reporting symptoms in both sets (from 27.0% to 46.3%). At the same time, the proportion reporting symptoms in only one set appears to decline (from 42.0% to 36.7%). However, among women reporting symptoms in one set the proportion reporting menopausal symptoms increases. The decrease in symptom reporting in postmenopausal women was again largely due to a decrease in combined symptom reporting (from 46.3% to 37.7%), with reporting of one set only remaining essentially unchanged at approximately 38%.

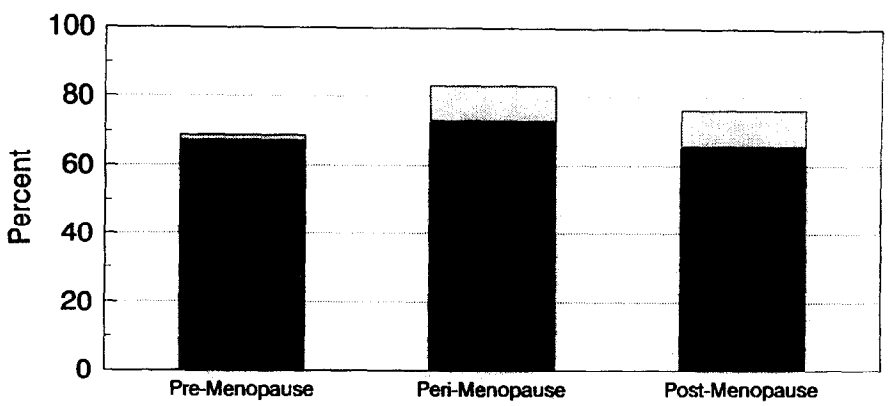

Fig. 2. Symptom reporting by menopause status at T_6 (n = 1178). ■, Menopause and other symptoms; ▩ other symptoms only; ▨ menopause symptoms only (hot flashes, sweats or insomnia).

The proportion reporting hot flashes was calculated in the premenopausal subcohort at each contact (T_i) within each transition state. The abscissa in Fig. 3 was coded by number of contact points before and after the two major transitions. Reading from left to right, the first three points (−3, −2, −1) represent the number of contacts (interviews) before the perimenopause transition is defined. Up to three contacts before this event are considered, only, as providing sufficiently stable estimates. Similarly, the next four points (−3, −2, −1, 0) represent contacts during perimenopause, before and including the transition to postmenopause (i.e. menstruation ceases just before perimenopausal point −1). The discontinuity between the pre- and perimenopausal points reflects the variation in duration of the perimenopause in this cohort. For example, the nearly 10% who experience short perimenopauses can contribute to up to all three premenopausal points in the figure, but only to one perimenopausal point (−1). The point at which perimenopause is defined is therefore represented as a point of discontinuity as it is imbedded in these four points. The last four points include those contacts following the definition of postmenopause (a maximum of 4 were observable as the second follow-up contact was, by definition, the earliest point at which women could be classified as postmenopausal).

Three contacts (27 months) before perimenopause is defined, the rate of hot flashes is approximately 10%, which can be considered to represent a baseline population rate for this phenomenon (hot flashes are not exclusive to women or to menopause). This rate increases slowly before the transition to perimenopause. Reporting frequency increases during the perimenopause to a peak of about 50% just after cessation of menses. By the fourth postmenopausal contact (approx. 4 years after LMP) the rate of hot flashes has declined to 20%. This decline represents 75% of the difference between baseline and peak rates.

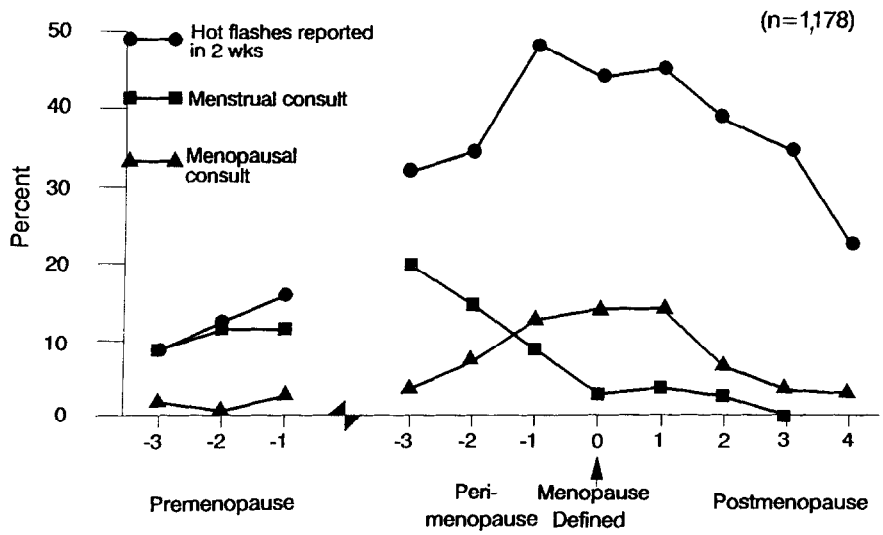

Fig. 3. Relationship between hot flashes reported in 2 weeks and physician contact for menstrual problems or menopause symptoms in 9 months (n = 1178).

This study also provides some evidence that the rate of hot flash reporting is related to the duration of the perimenopause. In particular, women who were perimenopausal for only one contact were consistently less likely to report hot flashes before, during and after the menopause than were women with a longer perimenopause. For example, among women with a short or no perimenopause, the percentage reporting hot flashes reached a maximum of 39% as compared with the remainder reporting a maximum of 51%, which occurred in the last perimenopausal contact. The rate of hot flash reporting remained higher among those with a longer perimenopause, at least through the first one or two postmenopausal contacts.

Finally, to demonstrate the lack of association between this major sign of menopause and efforts to seek medical care, two additional rates were estimated and superimposed on Fig. 3. Women in the cohort were asked if they had seen or talked to a physician since the previous interview in connection with menstrual or menopausal concerns. If a positive response was given the exact reason for the (most recent) contact was recorded and post-coded. Reasons which involved acute menstrual problems only were included as 'menstrual consult'. Those reasons that included bothersome hot flashes or more vaguely worded 'menopausal symptoms' were coded as 'menopausal consult'. Consultations motivated by information seeking rather than a need for acute symptom relief were not included.

Even though the consultation rates reflect a period of 9 months, and the hot flash reporting was for a period of only 2 weeks, the parallel trends in hot flash reporting and menopausal consults is remarkable. The large difference in rates is somewhat misleading, as women may consult a physician only once, even though the symptom persists for several months or years. When all women in the subcohort who reported hot flashes at least once during the perimenopause were investigated, nearly 50% reported a menopausal consult in the same period, compared with 33% who did not report hot flashes. These rates probably still represent overestimates of consultation for hot flashes specifically, since the definition used includes broader 'menopausal symptom' codes. The rate of reporting of menopausal consults among those with hot flashes also varied with the number of perimenopausal contacts, from 25.6% for those with one perimenopausal contact to 58% for 5–6 such contacts. The rate of menstrual consults peaks in those with a longer perimenopause, providing some validation of the definition of perimenopause used. The continuing very low rate of menstrual consults after the menopause reflects some reporting (memory) error as well as concerns with isolated bleeding or renewed cycling as a result of combined hormone therapy.

Discussion

This paper has presented, for the first time, information on the entire transmenopausal process in a general, community-dwelling, representative sample of women.

Prior reports have focussed on the time (age) of LMP, factors affecting this transition point and symptoms associated with it. Most of the inconsistent reporting of age at LMP in cross-sectional data sets has been due to two overriding methodological problems such as the use of self-reported menopause status based

on such questions as 'have your periods stopped?', and asking women to remember when (the year) their periods stopped naturally. Logit or probit transforms used on the proportions resulting from the first question produce an underestimate of the median age, since women tend to assume periods have ceased permanently after as few as 3 months of amenorrhea. This was the reason for the low U.S. estimate reported by MacMahon and Worcester (1966) using National Health and Examination Survey data [21]. The retrospective reports of year of LMP were used to calculate mean LMP in several reports and the resulting estimates were consistently lower than the medians. The presence of negative bias in these estimates was identified by McKinlay et al. [22].

The mean of 49.5 years calculated by Treloar [6] from prospective data was negatively biased as no adjustment was made for censored data.

There has also been inconsistent reporting of factors affecting the timing of LMP, primarily because prior analyses have not adjusted simultaneously for correlated factors [13]. These prior studies have also been based on very different samples of women, including convenience samples from screened, clinic or referral populations. Despite these difference, current cigarette smoking has been consistently implicated as having an immediate and sizeable effect on timing of LMP. This effect, represented by a median shift of about 1.5 years, was confirmed in the MWHS data sets, both cross-sectionally and longitudinally. The MWHS data were not able to confirm a dose-response relationship reported elsewhere, possibly because of measurement error (quantity smoked was pre-coded into only three categories [8]).

The strong effect of smoking on LMP is consistent with the results of animal studies [23] as well as with studies reporting higher rates of menstrual irregularity [24] and infertility [25,26] in smokers than in non-smokers. All of these results indicate an immediate toxic impact of the by-products of smoking on ovarian function.

The new analyses reported here on age at inception of perimenopause and factors affecting it are consistent with findings for age at LMP, particularly the overwhelming effect of smoking. Smokers tend to have not only an earlier but also a shorter perimenopause.

The length of the perimenopausal transition (estimated at nearly 4 years) has not been previously reported. Moreover, the highest rate of physician consults is observed among those with longer perimenopause transitions. The reported irregular (and frequently more heavy) menstrual bleeding, interspersed with periods of amenorrhea in this transition appear to be more worrisome to women than hot flashes — particularly if they last beyond a year or two. An important finding is that nearly 10% of women do not experience perimenopause, but abruptly cease menstruation and report lower rates of hot flashes.

The relationship between menopause transitions and symptom reporting appears to be transitory, with reporting rates showing an increase in the perimenopause. The finding that all symptomatology rather than just menopause-related symptoms increases temporarily is counter-intuitive and appears to negate prior multivariate analyses completed on cross-sectional data [14,16–19] as well as univariate analyses of longitudinal data [5], which indicate that hot flashes are the primary symptoms related to menopause and that other symptoms are related to each other, not to menopause. It may well be, following the thesis of Neugarten and Kraines [27], that

there is an identifiable subgroup of women who are susceptible to high rates of symptom reporting, particularly when confronted with a major physiological change such as menarche or menopause.

Apart from the substantive findings presented here, two methodological issues should be highlighted. First, the complexity of the analyses presented underscores the importance of large numbers, so that stable estimates can be obtained. Even with a cohort of over 1100 initially premenopausal women and 5 years of observation, numbers were barely sufficient to provide a reliable estimate of the parameters of menopause transition and their covariates.

Second, it should be reiterated that the low rates of hormone therapy in this Massachusetts study enabled observation of the natural transitions without HRT effects. If HRT (especially cyclically administered combined estrogen-progestogen therapy) is increasingly prescribed in the perimenopause, then the MWHS cannot be replicated in most western societies, as both transitions will be obscured by the appearance of regular cycling. A similar phenomenon has occurred in relation to the natural history of blood pressure levels in an aging population. The Framingham Heart Study [28] was one of the last prospective studies which documented changes with age in untreated blood pressures. All recent and ongoing blood pressure studies in western societies must now accommodate severely truncated distributions due to increasingly effective and pervasive treatment.

Acknowledgement

Supported by the National Institute on Aging, NIH, Grant No. AG0311.

References

1 National Center for Health Statistics. Annual summary of births, marriages, divorces, and deaths, United States, 1986. Monthly Vital Statistics Report Vol. 35, No. 13 DHHS Pub. No. (PHS) 87–1120. Public Health Services, Hyattsville, Md., August 24, 1987.

2 McKinlay SM, McKinlay JB. Selected studies of the menopause a methodological critique. J. Biosoc. Sci. 1973; 5: 533–555.

3 Holte A, Mikkelsen A. Menstrual coping style, social background and climacteric symptoms. Psychiatry Soc Sci 1982; 2: 41–45.

4 Kaufert P. Women and their health in the middle years: a Manitoba project. Soc Sci Med 1984; 18: 279–281.

5 Matthews KA, Kuller LH, Meilahn EN, Kelsey SF, Costello EJ, Caggiula AW. Influences of natural menopause on psychological characteristics and symptoms of middle-aged healthy women. J. Consult. Clin. Psychol. 1990; 58: 345–351.

6 Treloar AE. Menarche, menopause and intervening fecundability. Hum Biol. 46: 89–107, 1974.

7 Brambilla D, McKinlay SM. A comparison of responses to mailed questionnaires and telephone interviews in a mixed mode health survey. Am J Epidemiol 1987; 126 (5): 962–997.

8 Brambilla DJ, McKinlay SM. A prospective study of factors affecting age at menopause. J Clin Epidemiol, 1989; in press.

9 Brambilla DJ, McKinlay SM. A comparison of response to telephone and face-to-face interviews in a longitudinal study. Accepted for presentation at the 1989 Public Health conference on Records and Statistics and to be published in Conference Proceedings, 1989.

10 Brambilla D, McKinlay SM, McKinlay JB. Item Nonresponse and Response Bia in Mixed Mode Surveys. In Proceedings of the 1987 Public Health Conference on Records and Statistics. DHHS Pub. No. (PHS) 88–1214.

11 Brambilla DJ, McKinlay SM, Bifano N, and Clapp R. Validation of self-reported cancer incidence. Accepted for presentation at Fifth Conference on Health Survey Research Methods and to be published in the Conference Proceedings, 1989.

12 World Health Organization Scientific Group. research on Menopause. WHO Technical Service Report Series 670. Geneva: World Health Organisation; 1981.

13 McKinlay SM, Bifano NL, McKinlay, JB. Smoking and age at menopause. Ann Intern. Med. 1985; 103 (3): 350–356.

14 McKinlay SM, Jefferys M. The menopausal syndrome. Br J Prev. Soc. Med. 1974; 28: 108–115.

15 Krailo MD, Pike MC. Estimation of the distribution of age at natural menopause from prevalence data. Am J Epidemiol 1983; 117: 356–361.

16 Thompson B, Hart SA, Durno D. Menopausal age and symptomatology in a general practice. J Biosoc Sci, 5: 71, 1973.

17 Greene JG. A factor analytic study of climacteric symptoms. J Psychosom Res 1976; 20: 425–440.

18 Greene JG, Cooke DJ. Life stress and symptoms at the climacterium. Br J Psychiatry 1980; 136: 486–491.

19 Mikkelsen A, Holte A. A factor-analytic study of climacteric symptoms. Psychiatry Soc Sci 1982; 2: 35–39.

20 Schiff I, Regestein Q, Tulchinsky D, Ryan KJ. Effects of estrogens on sleep and psychological state of hypogonadal women. J Am Med Assoc 1979; 242 (2): 2405–2407.

21 MacMahon B, Worcester J. Age at menopause: United States 1960–1962. US Vital and Health Statistics, II 1966; 19:1–19.

22 McKinlay SM, Jefferys M, Thompson B. An investigation of the age at onset of the menopause. J Biosoc Sci 1972; 4: 161–173.

23 Mattison DR. The mechanisms of action of reproductive toxins. Am J Ind Med 1983; 4: 65–79.

24 Hammond EC. Smoking in relation to physical complaints. Arch Environ Health 1961; 3: 28–46.

25 Olsen J, Rachootin P, Schiodt AV, Damsbo N. Tobacco use, alcohol consumption and infertility. Int J Epidemiol 1983; 12 (2): 179–184.

26 Baird DD, Wilcox AJ. Cigarette smoking associated with delayed conception. J Am Med Assoc 1985; 253: 2979–2983.

27 Neugarten BL, Kraines RJ. Menopausal symptoms in women of various ages. Psychosom Med 1964; 27: 266–273.

28 Shurtleff D. Some characteristics related to the incidence of cardiovascular disease and death: Framingham Study, 18-year Follow up. Section 30. In: Kannel WB, Gordon T, eds. The Framingham Study: An Epidemiological Investigation of Cardiovascular Disease. Washington, DC: Government Printing Office, 1973. DHEW Pub. No. (NIH) 74–599.