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Marital Status and Age at Natural Menopause: Considering Pheromonal Influence

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ABSTRACT Married women generally report a later mean age at menopause. The results reported here, from a study carried out in Greene County, New York, are no exception. Married and widowed women report a later mean age at natural menopause compared to single and divorced women ($P < 0.05$). To better understand the relationship between marital status and age at menopause, possible mechanistic and confounding variables are examined, in particular parity, sexual activity, smoking habits, level of education, and income. Parity and income 10 years prior to interview are significant factors, along with marital status, that explain part of the variation in age at natural menopause. An alternative explanation is the pheromonal influence of a male in the household. This would explain the consistency of results across populations. This pilot study supports further biochemical investigation. *Am. J. Hum. Biol.* 13:479–485, 2001. © 2001 Wiley-Liss, Inc.

Studies across a variety of countries report later ages at natural menopause among married or widowed women compared to never married or divorced women (Jaszmann et al., 1969; McKinlay et al., 1972; Brand and Lehert, 1978; Neri et al., 1982; Stanford et al., 1987). Table 1 demonstrates the consistency of results reported by studies that apply a variety of methods. The direction of the relationship is always the same, i.e., women who are single at interview report an earlier age at menopause (MacMahon and Worcester, 1966; Brambilla and McKinlay, 1989; Parazzini et al., 1992; Shinberg, 1998). This consistency of association between marital status and age at menopause begs a biologically plausible explanation. By what mechanism could marriage have such an effect?

Age at menopause is determined by the number of oocytes (eggs) in the ovaries at birth coupled with the rate of follicular atresia (degeneration of pre-ovulatory follicles) across the lifespan (Gosden, 1985; Gougeon, 1996). When the quantity of follicles remaining falls below a threshold number, menstruation ceases (Nelson and Felicio, 1985; Wood et al., 1994). The rate of follicular atresia is affected by the chemical, immunological, and hormonal environment of the ovary (Guraya, 1985; Crisp, 1992; Leidy, 1994).

The effect of marriage on age at menopause may be brought about by biobehavioral factors that alter the internal hormonal or chemical environment, e.g., sexual

activity, parity, or smoking habits. The effect of marriage may also be confounded by the less direct influence of household income. An explanation that has not yet been considered is the pheromonal influence of the continued presence of a male in the household. The effects of primer pheromones—those that stimulate a delayed physiological or behavioral response (Weller, 1998)—have been documented in a variety of primates, including prosimians (Mertl, 1975), platyrrhines (Ziegler et al., 1987), macaques (Rogel, 1978), baboons (Colmenares and Gomendio, 1988), and humans (Porter and Moore, 1981; Cutler et al., 1986b; Gustavson et al., 1987; Wedekind et al., 1995). A review of this literature suggests that monogamous marriage, the equivalent of being housed with a male, could provide an alternative, biological explanation for the association consistently found between marriage and a later age at natural menopause.

METHODS

Data for this paper were drawn from a study of age at menopause and symptom experience carried out in Greene County, New York, 1989–1990. Data were gathered

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TABLE 1. Age at menopause by marital status

Study (source)	Marital status	Menopause		
Multicenter, USA, 1973–1980 (Stanford et al., 1987) Ages 26–62	Never married	Median age at natural menopause		<i>P</i> < 0.01
	Ever married	50 years 1 month	51 years 2 months	
USA, 1960–1962 (MacMahon and Worcester, 1966) Ages 18–79	Never married	49.91		n.s.
	Ever married	50.02		
Ede, Netherlands, 1967 (Jaszmann et al., 1969) Ages 42–62	Not married Married Widowed	Mean recalled age at natural menopause		<i>P</i> < 0.05
		50.3		
		51.4		
Ede, Netherlands, 1977 (Brandt and Lehert, 1978) Ages 40–60	Single/Divorced	48.3		<i>P</i> < 0.05
	Married/Widowed	49.6		
Milan, Italy, since 1983 (Parazzini et al., 1992) Ages 55–74	Never married	49.0		n.s.
	Ever married	49.4		
Israel, 1969 (Neri et al., 1982) Mean age 54.3 (±7.2 yr)	Single	48.3 (3.5)		<i>P</i> < 0.05
	Married	49.4 (2.9)		
	Divorced	48.4 (2.3)		
	Widowed	49.3 (2.7)		
Massachusetts, 1981–1982 (Brambilla and McKinlay, 1989) Ages 45–55	Never married	Likelihood ratios (multivariate models)		n.s.
	Ever married	2.71		
Wisconsin, 1992–1993 (Shinberg, 1998) Ages 53–54	Never married	1.17		n.s.
	Ever married			
London, Britain, 1965 (McKinlay et al., 1972) Ages 45–49	Not married Currently married	Percent post-menopausal		<i>P</i> < 0.05
		Non-manual	Manual ^a	
		32.4%	35.0%	
		12.0%	22.3%	

^aBased on husband's occupation or the woman's own if not married.

through interviews, anthropometry, and surveys administered to an opportunity sample of 376 women ages 39–82 years. Mean age at interview was 51.4, 92% of the sample were between 40 and 65 years. Women were self-selected from school districts (teachers and staff), health care settings (nurses and allied staff), county offices, and community organizations such as firehouse auxiliaries and garden clubs. Of the 376 women interviewed, 83% returned standardized surveys by mail. The resulting sample was skewed toward well-educated White women, 77% of whom were married.

Twenty-one percent of 240 married women, 24% of 29 widows, and 12.5% of 16 divorced women reported menopause by hysterectomy. No single women in the Greene County sample reported a history of hysterectomy; therefore, for the following analyses of age at natural menopause,

women who experienced menopause by hysterectomy were excluded.

Menopause was defined as the cessation of menstruation followed by at least 12 months of amenorrhea (Kaufert et al., 1987; WHO, 1996). Among naturally post-menopausal women, 104 remembered the year (or month/year) of their last menstrual period. Recalled age at menopause was determined by subtracting date of birth from date of last menstrual period. The similarity between mean recalled age at menopause and median age at menopause (see below) as determined by probit analysis (Finney, 1962) indicates a low degree of error in recall in this population (Horwitz and Yu, 1985; Colditz et al., 1987).

No selection was made on the basis of hormone replacement therapy because age at natural menopause did not significantly dif-

TABLE 2. Variation in demographic and bio-behavioral variables by marital status among women who reported a natural menopause after age 39 (Greene County, NY, 1989–1990)

	Married (<i>N</i> = 68)	Single (<i>N</i> = 10)	Divorced (<i>N</i> = 10)	Widowed (<i>N</i> = 12)
Mean age (SE)*	56.3 (0.8)	58.4 (2.2)	52.0 (2.1)	61.2 (1.9)
Mean age at natural menopause* (SE)	50.3 (0.4)	48.2 (1.1)	48.1 (1.1)	51.9 (1.0)
Mean BMI (SE)	29.0 (0.8)	30.2 (2.4)	27.8 (2.2)	23.8 (2.0)
Mean sexual activity per week (SE)	1.4 (0.2)	0.7 (0.5)	0.8 (0.5)	2.2 (0.5)
Mean parity (SE)	3.5 (0.2)	1.0 (1.7)	3.3 (0.6)	3.7 (0.5)
Family income, percent >\$40,000/year*	42%	10%	11%	8%
Family income 10 years ago, % >\$40,000/year	10%	0%	0%	9%
Nulliparous*	6%	90%	10%	0%
Employed full time	63%	80%	80%	58%
Education > HS	57%	90%	60%	33%
Smokers	19%	30%	50%	8%
Use HRT	9%	10%	10%	17%

* $P < 0.05$.

fer between those using HRT (50.9 years, $n = 10$) and those not using HRT (49.8 years, $n = 87$). Of the 104 naturally post-menopausal women, 100 experienced menopause after the age of 39. The results that follow are based on these 100 women.

Marital status was assessed with the question: What is your present marital status (single, married, divorced, widowed, other)? This was followed by: If you are now single due to death, divorce or separation, for how many years have you been single? Mean ages at natural menopause were compared by ANOVA across four categories of marital status (single, married, divorced, widowed). Two women who described themselves as “separated” were included in the divorced category.

Mean age at natural menopause differed in relation to marital status. Therefore, characteristics of women by marital status were examined for significant differences. Current family income and family income 10 years prior to interview were grouped into \$10,000 increments from less than \$10,000/year to more than \$40,000/year. Nulliparity, full-time employment status, formal education beyond high school, and present smoking habits were categorized as yes/no. Income, nulliparity, employment status, education, and smoking habits were tested in relation to marital status by Chi-square analyses. Age at interview, age at natural menopause, BMI (kg/m^2), sexual activity (measured as episodes of sexual intercourse per week at time of interview), and parity were examined in relation to marital status using ANOVA. Significant results are indicated by asterisks in Table 2.

In addition to marital status, other fac-

tors possibly related to age at menopause were examined. Family income at interview, income 10 years prior to interview, parity, sexual activity, education level, and smoking habits were tested in relation to age at menopause by Chi-square (for categorical variables) and ANOVA (for continuous variables) techniques.

Separate analyses of covariance (ANCOVAs) of age at menopause were run to evaluate the relationship between marital status and each of the following variables: parity, sexual activity, income at interview, and income 10 years prior to interview. Smoking habits (yes/no) and level of education (<13 years, 13–16 years, >16 years) were each separately examined as main effects along with marital status to explain variation in age at natural menopause. Finally, variation in age at menopause was examined with marital status as the main effect and parity and income 10 years prior to interview as covariates.

RESULTS

Mean age at natural menopause in this sample is 50.1 years (SD 3.6); median age at menopause, by probit analysis, is 50.0 years. Married and widowed women in Greene County, NY, report a later mean age at natural menopause than single and divorced women (Table 2).

Table 2 summarizes significant differences among study variables in relation to marital status. Of the women sampled, widowed women are the oldest and divorced women the youngest ($P < 0.05$). Married women are most likely to report a family income in excess of \$40,000 ($P < 0.05$). Single women are more likely to be nullip-

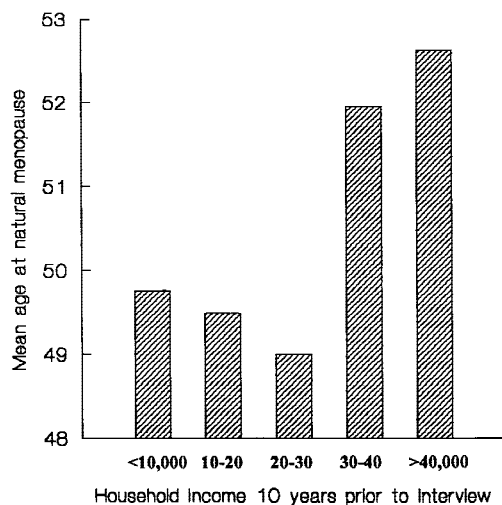


Fig. 1. Mean age at natural menopause in relation to family income 10 years prior to interview. Those with the highest income have the latest age at menopause ($P < 0.05$).

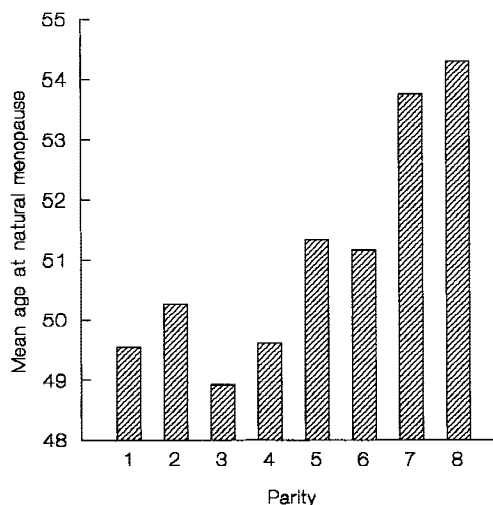


Fig. 2. Mean age at natural menopause in relation to parity. Women with 5–8 children have a significantly later age at menopause compared to women with 1–4 children ($P < 0.01$).

arous ($P < 0.05$). Widowed women report the least amount of formal education and single women the most ($P = 0.06$). Widows are much less likely to smoke ($P = 0.09$).

Age at menopause is positively correlated with age at interview ($r = 0.38$, $P < 0.01$). Age at menopause is not associated with family income at interview; however, family income 10 years prior to interview is significantly associated with age at menopause, so that those with the highest income have the latest age at menopause ($P < 0.05$, Fig. 1). Mean age at menopause does not significantly vary between parous and nulliparous women (50.3 vs. 48.8); however, mean age at menopause increases with parity so that women with 5–8 children have a significantly later age at menopause (52.1, SD 3.7) compared to women with 1–4 children (49.6, SD 2.6, $P < 0.01$, Fig. 2).

Age at menopause is not associated with sexual activity or education. Consistent with the literature on age at menopause, smokers have a significantly earlier mean age at menopause in the Greene County sample. Smokers report a mean age at menopause of 48.6 (SD 3.0) compared with 50.5 (SD 3.7) for nonsmokers ($P < 0.05$).

In covariate models, marital status remains significant as a factor explaining variance in age at menopause in combination with income at interview, income 10

years prior to interview, parity, sexual activity, and level of education (Table 3). Marital status is no longer significant in relation to age at menopause when combined with smoking habits. Marital status, parity, and family income 10 years prior to interview explain 31% of the variation in age at menopause.

DISCUSSION

A number of studies in a variety of populations have demonstrated a significant relationship between marital status and age at menopause. In this study mean age at menopause is significantly later among married and widowed women compared to single and divorced women. This difference is not explained by different rates of hysterectomy. When median age at menopause was computed by life table analysis (Lee, 1980), using age at hysterectomy as censored observations (Stanford et al., 1987), the same significant difference in age at menopause in relation to marital status remained (Leidy, 1999).

In the study reported here, sample sizes are very small and marital status is complicated by its changeability (see, for example, ten categories of marital history identified in a study of women at midlife in Israel; Datan et al., 1981:142). In the Greene County sample, six women who were wid-

TABLE 3. Analyses of covariance of age at menopause with marital status as a main effect; additional main effects and covariates are listed

Main effect	F value	Covariate(s)	F value
Marital status	3.3*	Income at interview	0.5
Marital status	2.8*	Income at 10 years prior to interview	4.4*
Marital status	3.4*	Parity	4.5*
Marital status	3.5*	Sexual activity	1.5
Two main effects			
Marital status	$F = 1.2$	and Smoking habits	$F = 1.9$
Marital status	$F = 4.1^*$	and Education categories	$F = 0.8$
Main effect and two covariates			
Marital status	$F = 3.2^*$	Parity	$F = 10.1^{**}$
		Income 10 years prior to interview	$F = 9.9^{**}$

* $P < 0.05$.

** $P < 0.01$.

ows at interview were married at the time of natural menopause, six were single for 3–22 years prior to menopause. The 10 women who were divorced at interview were single for 1.7–19.5 years prior to menopause. There was no correlation between the amount of time spent single and age at menopause. On the other hand, no correlation could be tested between amount of time spent married and age at menopause because women were asked neither the duration of their marriage nor whether this marriage was their first. There is no way to know if the married women were married at time of menopause. Given these methodological complications, it is even more interesting to return to the observation that prompted this study—that women who are single at time of interview consistently report an earlier mean or median age at menopause compared to women who are married at time of interview (Table 1).

An immediate inclination may be to suggest sexual activity as a causal connection between marital status and age at menopause (Jaszmann et al., 1969; McKinlay et al., 1972). Women who are sexually active at least once a week demonstrate higher levels of estrogen compared to less sexually active women (Cutler et al., 1986a). Of concern to this study, however, is the finding that marital status does not necessarily correspond to frequency of sexual activity. In fact, among sexually active women in the Greene County sample, widows reported the most frequent rate of sexual intercourse (difference not significant, Table 2). In addition, sexual activity at time of interview is not related to age at menopause.

Stanford et al. (1987) suggest that parity and oral contraceptive use explain the effect

of marriage on age at menopause. In this sample, oral contraceptive use was low and not variable (12% of married women and single women used the Pill). Mean age at menopause did not significantly differ between parous and nulliparous women, but did differ between women who bore 1–4 children compared to 5–8 children (Fig. 2). In covariate analyses, parity and marital status both explain part of the variance in age at natural menopause.

Smoking habits may explain part of the relationship between marital status and age at menopause. In this study smokers report an earlier mean age at menopause, and single and divorced women are more likely to smoke. The effect of smoking can be explained in biologically plausible terms because nicotine may affect the function of the ovaries through effects on the circulatory system (Gosden, 1985) and cigarette smoke has been shown to destroy primordial oocytes in the mouse ovary in a dose-related way (Mattison and Thorgeirsson, 1978). However, when marital status and smoking habits were combined in an analysis of covariance, neither one explained enough of the variance in age at natural menopause to be significant.

Income levels may play a confounding role, particularly as age at menopause varied significantly in relation to level of family income 10 years prior to interview. In covariate analyses, income 10 years prior to interview and marital status both explain part of the variance in age at natural menopause. However, unlike sexual activity, parity, or smoking habits, the relationship between income and age at natural menopause begs its own biological plausibility.

An alternative suggestion is that the

presence of a male in the household may affect, through pheromones, the hormonal milieu of the ovary, ultimately influencing age at menopause. This explanation was initially prompted by the observation that female rats housed with male rats demonstrate a longer cycling lifespan (Nass et al., 1982).

A pheromone is a chemical, or mixture of chemicals, released by an organism that causes specific reactions in an organism of the same species (Agosta, 1992). While pheromones released by invertebrates, fish, amphibians, and reptiles send messages of attraction or warning to an entire species, the pheromones of mammals are more individualized. The category of pheromones most closely related to the topic of menopause is a group called "primer pheromones." Primer pheromones do not trigger an immediate behavioral response, but exert "an indirect modifying influence" on the physiology of other individuals (Stoddart, 1976; Weller, 1998).

Among mice, the estrus cycles of females are suppressed by the proximity of, or soiled bedding of, other females (Champlin, 1971; Whitten, 1959) and estrus cycles are shortened and synchronized by the presence of a male or male urine (Whitten, 1958). The effect of male proximity on female reproductive cycles has also been demonstrated in rats (Vandenbergh, 1976), cotton-top tamarins (Windowski, 1990), Celebes black apes (Bernstein et al., 1982), and especially baboons (Colmenares and Gomendio, 1988).

That humans are, also, affected by pheromones has been suggested by studies of menstrual synchrony (Graham and McGrew, 1980; McClintock, 1971), kin recognition (Porter and Moore, 1981), restroom-stall choice (Gustavson et al., 1987), t-shirt odor and MHC similarity (Wedekind et al., 1995), the effect of boar androstenone and mink secretion odor on human menstrual cycles (Sokolov et al., 1992), and the effects of male and female axillary secretions on the timing of menstrual onset (Cutler et al., 1986b; Preti et al., 1986). In addition, the finding of the human vomeronasal organ (VNO), which in other mammals senses pheromones, provides further evidence that humans are also sensitive to pheromonal signals (Takami et al., 1993; Bartoshuk and Beauchamp, 1994).

How the presence of a male could be able to bring about a later age at menopause may

be explained by the increased likelihood of regular menstrual cycle lengths of 29.5 (± 3 days) associated with male pheromones (Cutler et al., 1986b). Women with median cycle lengths of 26–32 days experience menopause 1.4 years later, on average, than women with median cycle lengths of less than 26 days (Whelan et al., 1990).

In conclusion, the results of this study can be used to suggest that parity is a mechanism by which marriage influences age at menopause. Smoking habits that differ by marital status may also be the means by which marriage and menopause are associated, although in this study neither marital status nor smoking habits explain enough of the variance in age at natural menopause to be significant when combined in an analysis of covariance. Alternatively, past income levels appear to confound the effect of marriage on age at natural menopause. Finally, a broader species-wide perspective suggests pheromonal influences. Future work needs to more carefully characterize "housing" arrangements, ask more specific questions about marital and sexual patterns across the lifespan, broaden the definition of marriage to include all partnerships, lesbian as well as heterosexual, and incorporate biochemical indices of pheromonal influence. Such studies will continue to expand our knowledge about the interactions between biology and culture; in this case, the effect of marital status on the timing of natural menopause.

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