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Is the Menopausal Transition Stressful? Observations of Perceived Stress from the Seattle Midlife Women's Health Study

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Popular and medical literature about the menopausal transition (MT) reflects assumptions that it is stressful, but few investigators have actually evaluated perceived stress during this period in a woman's life. Menopause literature from the 1960s implicated the "empty nest" as a source of stress¹ whereas more contemporary literature reflects the challenges women face as they juggle the responsibilities of the workplace and their families with consequent overload and role burden². Although some assume that symptoms women experience during the MT are stressful, to date only Freeman and colleagues have examined the relationship of MT symptoms to perceived stress³. There are no publications examining the relationship of both biological aspects of the MT and the social dimensions of midlife to perceived stress.

Studies of midlife women have examined the social origins of stress. Walters⁴ investigation of 356 Canadian women revealed that those with more education, greater household sizes, single parenting responsibilities, paid employment, and employment in professional occupations reported the highest stress levels. Sources of stress included their children's health, parenting, relationship with a partner or family members, caring for sick or elderly relatives, combining work and parenting, lack of time for oneself, insufficient money, possible unemployment, lack of confidence, and lack of sleep. Walters concluded that women who were stressed were "trying to be everything everyone wanted them to be" and "putting out for others, but receiving little in return" and linked her findings to the cultural pressures for women to engage in gendered caring roles without access to support from the society.

Other contemporary studies of midlife women support that relationship with partners, children, and older family members needing caregiving figure prominently as sources of

stress⁵⁻⁷. In addition, demands of paid employment as well as worry about unemployment account for a great deal of stress⁸⁻⁹. Linked to worry about unemployment or underemployment is concern about financial resources.

Women confront stressors related to the material conditions of their lives, such as having an inadequate income to support basic needs. Early results from the Study of Women across the Nation (SWAN) revealed that difficulty paying for basics, lower educational attainment, and lack of full time employment were associated with reporting more symptoms by a midlife multi-ethnic sample from multiple sites in the United States¹⁰.

As women note their own aging, they also express worry about the health consequences of getting older^{6,7}. Deaths of contemporaries as well as parents become a source of stress during midlife⁷. As women confront their own aging and mortality lack of goal attainment may become a source of stress⁷.

For contemporary midlife women, role overload, role burden, and lack of support seem to play a unique role in precipitating stress. Amick and colleagues⁸ found iso-strain (high strain and low support at work) was prevalent among the Nurses' Health Study cohort and was associated with functional decline in several dimensions of health over four years of follow-up. Despite gains in the workplace, many women experience non-supportive work environments in which gender-specific occupational stressors such as inequitable treatment in hiring and promotion, salary differentials between women and men, limited career advancement opportunities, and sexual harassment persist.

Role overload occurs as a result of the disproportionate amount of work women undertake within the family sphere in addition to their paid employment. The "second shift" is a term used to capture the fact that women log a disproportionate number of hours once they return home from their paid employment when compared to men¹¹. Most of the additional work is brought about by responsibilities for nurturant caregiving, reflecting the traditional roles allocated to women: parenting and caregiving for the elderly or those with health problems. Studies of caregivers suggest that it is not what women do, but how they perceive caregiving affects their lives that is significant.¹²

Spillover effects of family to work and work to family stress are also prevalent among midlife women. Women lacking child care and household help from spouses and who work in demanding jobs may suffer poor health and lower well-being.¹³ Even among managers and professional specialists in high-ranking positions women were more stressed than men by their greater unpaid workload and by a greater responsibility for home and family. Women had higher norepinephrine levels than men did, both during and after work, and women with children at home had significantly higher norepinephrine levels after work than other participants.¹⁴

Support from partners can alleviate the sense of burden women feel.^{15,16} In addition to a lack of support from a spouse or partner, women may suffer sexual, psychological, and physical abuse by partner.¹⁷

Recent studies of depressed mood during the menopausal transition link negative life event stress as well as menopausal transition-related factors^{18,21}. To date, no studies have focused on the influence of depressed mood on perceived stress during this developmental stage of a woman's life.

The menopausal transition is a time of changing menstrual patterns, fluctuating hormonal levels, and bothersome symptoms for some women. In only one study of stressors among midlife women was there any mention of the MT as stressful, and this was rare.² Although

there are multiple studies of stress experienced by midlife women, to date none has examined the relationship of the MT in the context of other aspects of midlife to perceived stress.

The purposes of this paper are to:

1. assess whether perceived stress levels vary with menopausal transition-related factors, including MT stages, hot flash severity, urinary FSH and estrone glucuronide levels, and hormone therapy use; and
2. explore the relationships among perceived stress and psychosocial factors (social support, employment, role burden, income adequacy, parenting, sexual abuse, and depressed mood) and aging factors (physical appraisal and perceived health) during the MT and early postmenopause.

Methods

Design

The data for these analyses are part of a larger longitudinal study, the Seattle Midlife Women's Health Study. Women entered the cohort between 1990 and early 1992 when most were not yet in the MT or were in the early stages of the transition to menopause. After completing an initial in-person interview administered by a trained registered nurse interviewer, participants provided data annually by questionnaire, menstrual calendar, and health diary. In late 1996 a subset of the original cohort began providing 3-day monthly diary data as well as first morning voided urine specimens 8 to 12 times per year for endocrine assays (through 2000), and then quarterly for 2001-2005. These data were in addition to an annual health questionnaire and menstrual calendars.

Sample

Participants (N=418) were those who contributed at least one perceived stress score from health reports beginning in 1990 and were in the late reproductive, early and late menopausal transition stages, and early postmenopause during the course of the study. A subset of 133 women who contributed urine samples starting in 1996 were also included in the analyses. Women whose data were available for analysis were midlife women with a mean age of 41.3 (SD=4.3) years at the beginning of the study, 15.8 years of education (SD=2.9), and a median family income of \$37,200 (SD=\$15,800). Most (86%) of the participants were currently employed, 68% married or partnered, 25% divorced or separated, and 7% never married or partnered. Women described themselves as follows: 11% African American, 9% Asian American, 78% Caucasian. As seen in Table 1, women who were included in these analyses compared to those who were ineligible were similar with respect to family income, perceived stress, employment, race/ethnicity, and marital status. Those who were included in the analyses were slightly younger and slightly better educated than those who were ineligible.

Measures

The measures used for this study included perceived stress, age, MT stage, hot flash severity, urinary estrone glucuronide, and FSH. In addition, psychosocial factors included social support, income adequacy, employment, role burden, history of sexual abuse, depressed mood, and having had a live birth. Age-related factors included the appraisal of physical changes related to aging and perceived health.

Perceived Stress—Perceived stress was assessed in the health questionnaire administered annually. Stress related to physical health, job/student roles, family/parenting, and personal

life over the past month were measured. These items were rated such that 1 indicated no stress in the area and 4 indicated a lot of stress. The mean of the 4 items was used as the measure of perceived stress level. Brantly, Waggoner, Jones, & Rappaport²², found that a global stress rating and the sum of stress ratings across multiple dimensions correlated significantly ($r=.35$, $p<.01$).

Menopausal Transition-related Factors—Menopausal transition-related factors included MT stage, hot flash severity, urinary estrone glucuronide and urinary FSH. Using menstrual calendar data, women not taking any hormones were classified according to stages of reproductive aging: late reproductive, early menopausal transition, late menopausal transition, or early postmenopause, based on staging criteria developed by Mitchell, Woods and Mariella.²³ The names of stages match those recommended at the Stages of Reproductive Aging Workshop (STRAW)²⁴. The time before the onset of persistent menstrual irregularity during midlife was labeled the late reproductive stage when cycles were regular. Early stage was defined as persistent irregularity of more than 6 days absolute difference between any two consecutive menstrual cycles during the calendar year, with no skipped periods. Late transition stage was defined as persistent skipping of one or more menstrual periods. A skipped period was defined as double the modal cycle length or more for the calendar year. In the absence of a modal cycle length, a population-based cycle length of 29 days was used.²⁵ Persistence meant the event, irregular cycle or skipped period, occurred one or more times in the subsequent 12 months. Final menstrual period (FMP) was identified retrospectively after one year of amenorrhea without any known explanation. The date of the FMP was synonymous with the term menopause. Early postmenopause was within five years of the FMP.

Urinary Assays—Urinary assays were performed in our laboratories using a first-voided morning urine specimen provided on day 6 of the menstrual cycle, if menstrual periods were identifiable. For women with no bleeding or spotting or extremely erratic flow, a consistent date each month was used. Women abstained from smoking, caffeine use, and exercise before the urine collection. Urine samples were preserved with sodium ethylenediaminetetraacetic acid and sodium metabisulfite and frozen at -70°C . All specimens, standards and controls were tested in duplicate and those with a coefficient of variance above 15% were repeated. A BioRad Quantitative Urine control and a pooled in-house urine control were included in all assays, and a member of the standard curve was repeated after every ten unknowns to monitor assay performance. In general, all samples from a calendar year were assayed during the next calendar year and multiple samples from each participant were assayed in the same batch during each year. All endocrine concentrations were corrected for variations in urine concentration by expressing the hormone level as a ratio to the concentration in the same urine specimen.

Urinary estrone glucuronide (E_1G) was used for measuring estrogen because it is stable, can be reliably measured without special preparation, and is highly correlated with serum estradiol levels.²⁶⁻³¹ Urinary E_1G was measured by a competitive enzyme immunoassay (EIA) that cross-reacts 100% with E_1G , 83% with estradiol glucuronide and less than 10% with free estrone, estrone sulfate, estriol glucuronide, estradiol and estriol²⁸. The assay is described in detail elsewhere²⁸. Urinary E_1G concentrations estimated from this EIA were highly correlated with serum estradiol (Pearson's $r=0.95$; based on 30 averaged cycles).²⁸ The lower limit of detection for the assay was 3.1 nmol/L. Average recovery from a urine matrix of low, medium and high E_1G standard doses was 101%.²⁸ Intra- and inter-assay coefficients of variation (CV) were 2.1% and 9.6%, respectively, for an external (BioRad) urine control (mean concentration 2.1ng/mL); and 2.8% and 14.5%, respectively, for an internal urine control (mean concentration 1.59 ng/mL) (determined using the method of

Robard from 20 randomly selected plates).³² E₁G concentrations were corrected for slight assay non-parallelism²⁸ and standardized to a 1:5 dilution for all specimens.

Urinary FSH was assayed using Diagnostic Products Corporation (DPC) Double Antibody FSH Kit, using a radioimmunoassay (RIA) was designed for the quantitative measurement of FSH in serum and urine. The procedure is described in detail elsewhere³³. FSH levels used in the analyses were reported as mIU/mg creatinine. The reporting range for urine FSH was 2.0 to 100 mIU/mL; the minimum detectable concentration was 1.6 mIU. The inter-assay variation (run to run) was 7.1% and the intra-assay variation (within run) was 3.7% (N=205).

Urinary creatinine was assayed in urine specimens using the method of Jaffe³⁴. The inter-assay variation (run to run) was 6.7% and the intra-assay variation was 3.1% (N = 405).

Hot flash severity was assessed annually from 1996 to the end of the study by asking women if they had experienced hot flashes during the past three months. Women rated the severity of their hot flashes, from 1, minimal, to 4, severe.

Hormone therapy use was assessed in the annual health questionnaire and in the 3-day diaries. Use was coded 1 for “yes” or 0 for “no” for each time point.

Psychosocial Factors—Social factors included social support, role burden, employment, parenting, income adequacy and history of sexual abuse.

Social support was measured with a 6-item inventory covering ways that people provide support (being able to talk to someone about very personal and private matters, depend on people to lend or give \$50, get important advice from others, receive time and energy from others to help take care of something, and get together with people for fun and relaxation). These areas were adapted from the Arizona Social Support Inventory by Barrera³⁵. Instead of eliciting numbers of people in each area who might and actually did provide each type of support, this adapted version asks about current support availability for each area rated from 0 (not at all) to 3 (quite a bit). Cronbach's alpha for internal consistency reliability in this study was from 0.73 to 0.83 from 1997 to 2005.

Role burden was assessed using the Objective Burden Scale, a 9-item scale that asked women to rate items such as the amount of time they have to themselves and the amount of privacy they have. The ratings were made on a 5 point scale where 1 indicated that their situation was a lot worse and 5 a lot better than 12 months ago. The scale was developed to assess the burden associated with caregiving for elderly relatives and associated with indicators of caregiving tasks that confined the caregiver either temporally or geographically³⁶. For the Seattle Midlife Women's Health Study, the stem was: considering all of your different roles and functions in life and how you usually spend your time, tell me the amount each of the following areas in your life has changed from one year ago. Alpha levels ranged from .71 to .81 over all years in the SMWHS.

Employment was reported in the annual health questionnaire. Employment was coded as 1 for yes and 0 for no in the analyses reported here.

Parenting was reported as whether the woman had ever had a live birth. This was used as a marker for parenting status in the annual health questionnaire. This variable was coded as 1 for yes and 0 for no in the analyses reported here.

Sexual abuse history was assessed by asking “Have you ever been sexually assaulted, abused, or molested?” These data were obtained in 1999-2002. Also, beginning in 1996 and

through the end of the study, we asked “during the past year did you experience any sexual abuse or sexual assault?” A cumulative variable was created to represent any history of sexual abuse or assault and coded as 1 for yes and 0 for no.

Income adequacy was measured using the Income Adequacy Scale developed by Lobo³⁷. This scale assesses perceived adequacy of income for six areas of life: daily living, rent or mortgage, food bills, health care, recreation, and child care costs. Participants rated income as more than adequate (4) to not at all adequate (1). Ratings were averaged for a summary score. Cronbach's alpha levels were high (.88 to .95) over the course of the SMWHS.

Depressed mood was assessed using the Center for Epidemiologic Studies-Depression scale (CES-D), a 20-item self-report measure of depressive symptoms derived from clinical criteria for major depressive disorder (MDD). Categories included positive affect, negative affect, somatic, and interpersonal symptoms³⁸. Women rate how often they had a specific feeling during the past week on a 4-point scale from 0 [rarely or none of the time (less than 1 day)] to 3 [most or all of the time (5-7 days)]. The four items of the positive affect category are worded positively and are reverse coded for computation of total score. The total CES-D score is a sum of the ratings of the 20 items, ranging from 0 to 60. A cut-off of 16 has been used to differentiate depressed from non-depressed individuals^{6,7}. In Radloff's study³⁸, test-retest reliability correlations were .40 or above, and internal consistency reliability as measured by Cronbach's α was .80 or above. In the SMWHS study, α was .88 for the 508 women. The CES-D was administered annually for 15 years from 1990-2005.

Aging-related Factors included appraisal of physical changes related to aging and perceived health. Appraisal of physical changes was measured using the Aging Symptoms Inventory (ASI), originally developed to assess health among midlife women. ASI scores were found to be one of the best predictors of emotional closeness in relationships with adolescent children and maternal stress and exhaustion. Women responded to 9 items, including eyesight and shape of the body, rating themselves at the present time on a 10 point scale in which 0 was poor and 10 was excellent.³⁹ Alpha levels ranged from .64 to .83 over the course of the SMWHS.

Perceived health was measured in the annual health questionnaire from 1995 to the end of data collection using the item asking women to rate their current health on a scale ranging from poor (0) to excellent (10).

Analyses

Mixed effects modeling using the R library⁴⁰⁻⁴⁴ was used to investigate whether age, MT stage, variables related to the menopausal transition and psychosocial and aging-related factors were significant predictors of perceived stress over time. Age was centered at the group mean to aid in interpretability. Details of the models (described briefly below) are provided in the Appendix.

The initial series of models tested age alone as a predictor of perceived stress. The first model postulated that overall levels of perceived stress scores could differ from woman to woman (random intercept), but the scores would change with age in a common manner (fixed slope). The second model extended the first to postulate a random slope for each woman. The best fitting model was assessed by using maximum likelihood estimation with Akaike Information Criterion⁴⁴. When the best fitting model was found we extended that model by adding covariates iteratively to test the effect on perceived stress scores over time. Each covariate, including stage, was initially added independently to the best fitting model. Finally, all covariates that significantly improved the model fit to the data when entered individually were added simultaneously into a final model. A p-value of .05 was used as the

criterion for significance. Different numbers of women and observations occurred with each variable tested because the analysis required pairing of observations of the outcome and predictor variables at each time point.

RESULTS

To enhance interpretability of results, age was centered at 47.9 years, the mean for the sample included in these analyses. The random intercept and random slope model for age proved to be a better fit for the data ($p < 0.001$) than a model using fixed slope. The average initial perceived stress level for the entire sample (intercept) at age 47.9 years was 2.2. There was a slight non-significant decrease in average annual rate of change in perceived stress scores as women aged (beta = -0.002 , $p = 0.50$). Because the Aikake criterion was lower for the random slope model than that for the fixed slope model, the random intercept, random slope model was then used as the model to which single covariates, including MT stage, were considered one at a time.

When added as covariates with age to a model to predict perceived stress, none of the menopausal transition-related factors (MT stages, urinary estrone glucuronide, urinary FSH, hormone use and hot flash severity) was significantly associated with perceived stress (See Table 2). Although the model with MT stage and age was not significantly associated with perceived stress ($p = 0.08$), there was a slight decrease in perceived stress during the early postmenopause (beta = -0.11 , $p = 0.06$).

In contrast to findings for MT factors, when added individually as covariates with age to the model, appraisal of physical aging changes and perceived health were significantly related to perceived stress. A more positive rating of aging changes was associated with a reduction in perceived stress (beta = -0.08 , $p < 0.0001$), as was more positive perceived health (beta = -0.08 , $p = 0.0001$).

In addition to MT-related factors and aging-related factors, we examined the relationships between individual psychosocial factors and perceived stress. Social support predicted a decrease in perceived stress (beta = -0.13 , $p < 0.0005$), as did income adequacy (beta = -0.10 , $p < 0.0001$). Increasing role burden was associated with a significant increase in perceived stress (beta = 0.19 , $p < 0.0001$), as was history of sexual abuse (beta = 0.11 , $p = 0.03$) and depressed mood (beta = 0.24 , $p < 0.001$). Although employment was associated with a significant increase in perceived stress (beta = 0.14 , $p < 0.0001$), having had at least one live birth was not significantly related to perceived stress (beta = 0.04 , $p = 0.37$).

When each of the significant covariates was included together in a model with age, depressed mood, employment, and perceived health were all associated significantly with perceived stress. History of sexual abuse, social support, income adequacy, role burden, and appraisal of physical changes were not. Of interest is that employment was associated with the largest effect on perceived stress level of all the covariates. (Table 3).

Discussion

Although some would anticipate that the MT would be experienced as stressful, when compared to the late reproductive period and early postmenopause (PM), there was not a dramatic increase in perceived stress during this period of women's lives. Instead, there was a slight decline in perceived stress levels during early PM relative to the late transition stage, but no significant rise associated with either the early or late MT stage. This finding is of interest because the late transition stage appears to be a period of vulnerability for women, with the most severe hot flashes and depressed mood recorded during this stage for the participants in the Seattle Midlife Women's Health Study^{18,45} In addition, perceived stress

levels were not related to hot flash severity scores, nor to endocrine levels (estrone and FSH) or hormone therapy use.

In contrast to the lack of effect of MT-related factors on perceived stress, psychosocial factors that have been related to perceived stress among women during earlier periods of the lifespan, when considered individually, were significant predictors during the MT and early PM. Employment was positively associated with perceived stress in this sample, with an effect much larger than that of any other individual covariate, including depressed mood. The importance of employment as a source of stress for midlife women may reflect the inherent demands of the work, itself, but may also be related to the overall role burden women bear. Indeed, role burden was significantly correlated with employment ($r=.12$) and also related to perceived stress when considered as a covariate with age. Given the nature of contemporary women's lives and the demands for contributing both in the labor market and the unpaid labor market of their families and communities, employment may represent a commitment of work that increases role burden^{4,8,10}. Employment's effects on dimensions of role burden, including the amount of time women have to themselves; privacy; personal freedom; energy; time to spend in recreational or social activities, vacation activities, relationships with other family members; and their ability to handle their roles and responsibilities may be reflected in employment effects on perceived stress. Income adequacy provided a direct estimate of how well women's earnings met their needs for housing, food, health care, recreation, child-rearing costs, and other daily needs. As anticipated, income adequacy had an important influence on perceived stress when considered as a covariate with age, reflecting the importance of material strain in women's lives^{4,10}. Employment was negatively correlated with income adequacy ($r=-.22$), suggesting that income inadequacy may have necessitated employment and that income earned did not counteract the stressful effects of employment. This is demonstrated when income adequacy is combined with employment in the final model: income adequacy is no longer significant when the effect of employment is considered..

Social support research has supported its stress- buffering effects on health outcomes⁴⁶. In the context of other factors, including employment, income adequacy, role burden, depressed mood, and perceived health, social support did not have a significant effect on perceived stress in this cohort of women experiencing the menopausal transition.

The relationship of history of sexual abuse to perceived stress was anticipated. To date there are no published reports of the impact of sexual abuse history on perceived stress during the MT, although there is a recent study linking a history of sexual abuse to hot flashes⁴⁷. These findings suggest that a sexual abuse history may serve as an indicator of chronic stress, and perhaps as a marker for post-traumatic stress disorder in some women. When history of sexual abuse was considered in a multivariate model of perceived stress along with role burden, employment, income adequacy, depressed mood, and perceived health in this set of analyses, history of sexual abuse did not have significant effects. Perhaps the relationship with depressed mood and current social factors in women's lives, such as the demands of employment and poor health, reflect its effects.

Aging effects, as reflected by the appraisal of physical aging changes and perceived health, when considered individually, were associated with increased perceived stress. When considered in a multivariate model, appraisal of physical aging changes was not significant. Instead, perceived health contributed to perceived stress. Perceived health may overshadow the appraisal of how one's body changes with age as a source of stress for midlife women.

Depressed mood was significantly associated with perceived stress in the final multivariate model as well as when considered individually. Given that negative affect is an important

dimension of depression, it is likely that women who suffer from depressed mood during the menopausal transition and early menopause experience their lives and the daily events in them as more stressful than women who are not troubled by depressed mood.

Finally, when all the covariates that were individually related to perceived stress were considered in a multivariate model, employment, depressed mood, and perceived health were most influential. Together, these three psychosocial factors overshadowed any effects of the menopausal transition. Moreover, their effects in the model rendered income adequacy, role burden, aging changes, social support, and history of sexual abuse no longer statistically significant. These results may reflect the effects of income adequacy, role burden, aging changes, social support, and history of sexual abuse on depressed mood such that depressed mood mediates their effects on perceived stress. This explanation would be consistent with our prior analyses of depressed mood across the menopausal transition which revealed that negative life event stress was significantly associated with CESD scores¹⁸.

Although it is tempting to conclude that women who experience the menopausal transition as stressful are those who become depressed during this period of their lives owing to changing biology, it is important to consider that other psychosocial factors loom as important in our data. Women who experience depressed mood, have poor health, and are employed seem to be the most “stressed out”, but they may become depressed because of situational factors, such as not feeling supported, having too much responsibility, and not enough money to meet their needs.

In summary, the most dramatic finding in this set of analyses was the lack of effect of the menopausal transition-related factors on perceived stress in this group of midlife women and the importance of psychosocial factors, particularly employment. Taken together, employment, depressed mood, and perceived health overshadowed any of the features of the MT. These findings suggest that clinicians should be alert to the psychosocial sources of stress in midlife women's lives and avoid attributing their stress perceptions to the MT without taking a detailed history including the broader context of their lives.

APPENDIX

Let y_{ij} represent the j th perceived stress score obtained from the i th woman, where $i = 1, \dots, M$ and $j = 1, \dots, n_i$. Here $M = 418$ is the total number of women who have at least one perceived stress score in one of the four stages, and n_i is the total number of perceived stress scores for the i th woman (while $n_i \geq 1$ for all i , the value of n_i varies from woman to woman). Let x_{ij} represent the corresponding age for the woman when the value y_{ij} was recorded. In the models below, x_{ij} is centered at 47.9, which is the approximate sample mean of all recorded ages.

The first age-based model assumes that

$$y_{ij} = \beta_1 + b_{1,i} + \beta_2 (x_{ij} - 46.5) + \varepsilon_{ij}, \quad (1)$$

where the fixed effect β_1 represents the mean perceived stress score at age 47.9 over the population of women; $b_{1,i}$ is a random variable (RV) that is normally distributed with mean zero and variance σ_1^2 (this RV represents the deviation from β_1 for the i th woman); β_2 is a fixed slope; and ε_{ij} represents the error terms, which are independent and normally distributed with mean zero and variance σ_2^2 (the RVs $b_{1,i}$ and ε_{ij} are assumed to be independent of each other). This model basically postulates that, while the overall levels of perceived stress scores can differ from woman to woman, the scores change with age in a common manner.

The second model differs from the first in that it postulates a random slope for each woman:

$$y_{ij} = \beta_1 + b_{1,i} + b_{2,i}(x_{ij} - 46.5) + \varepsilon_{ij}, \quad (2)$$

where β_1 , $b_{1,i}$ and ε_{ij} are interpreted in the same manner as the first model, while $b_{2,i}$ is an RV representing the slope associated with the i th woman. We assume that $b_{2,i}$ is normally distributed with mean μ_2 and variance σ_2^2 . The RVs $b_{1,i}$ and ε_{ij} are assumed to be independent of each other, as are $b_{2,i}$ and ε_{ij} ; however, $b_{1,i}$ and $b_{2,i}$ are allowed to be correlated. This model basically postulates both the overall levels of perceived stress scores and their slopes can differ from woman to woman.

The third model extends the second by adding one or more covariates. In the case of a single covariate Z_{ij} , the model takes the form

$$y_{ij} = \beta_1 + b_{1,i} + b_{2,i}(x_{ij} - 46.5) + \beta_{3,i}Z_{ij} + \varepsilon_{ij}, \quad (3)$$

where $\beta_{3,i}$ is a fixed effect associated with Z_{ij} . Additional covariates are added in an obvious way.

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Table 1

Sample Characteristics of the Eligible and Ineligible Women in the Mixed Effects Modeling Analyses of Perceived Stress at Start of Study (1990-1991).

Characteristic	Eligible Women (n=418)	Ineligible Women (n=90)	p value *
	Mean (SD)	Mean (SD)	
Age (years)	41.3 (4.3)	43.3 (5.9)	0.004
Years of education	15.8 (2.9)	15.2 (2.8)	0.08
Family income (\$)	37,200 (15,800)	35,600 (18,000)	0.40
Perceived Stress (mean)	2.21 (0.5)	2.27 (0.52)	0.35
Characteristic	N (Percent)	N (Percent)	p value **
Currently employed			0.89
Yes	360 (86.1)	78 (86.7)	
No	58 (13.9)	12 (13.3)	
Race/ethnicity			0.15
African American	46 (11.0)	12 (13.3)	
Asian /Pacific Islander	37 (8.9)	6 (6.7)	
Caucasian	325 (77.7)	66 (73.3)	
Other (Hispanic, Mixed)	10 (2.4)	6 (6.7)	
Marital Status			0.95
Married/partnered	285 (68.2)	63 (70.0)	
Divorced/widowed	104 (24.9)	21 (23.3)	
Never married	29 (6.9)	6 (6.7)	

* Independent t-test

** Chi-square test

Table 2
Random Effects Models for Perceived Stress (1) with Age as Predictor (2) and with Individual Covariates (3)

Predictor	Mean Values (p values)			Standard Deviations			Number	
	1 *	2 *	3 *	1 **	2 **	**	Women	Observations
MT-stage	2.25 (<0.0001)	0.002 (0.57)		0.33	0.02	0.42	418	1814
Early			-0.05 (0.17)					
Late			-0.008 (0.85)					
Early PM			-0.11 (0.06)					
Hot flash severity	2.22 (<0.0001)	-0.006 (0.16)		0.32	0.03	0.40	202	1276
Estrone glucuronide (log ₁₀)	2.23 (<0.0001)	-0.04 (0.61)	.03 (0.62)	0.31	0.04	0.38	132	566
FSH (log ₁₀)	2.23 (<0.0001)	<0.005 (0.48)		0.31	0.04	0.38	132	566
HRT Use	2.21 (0.00)	-0.003 (0.24)		0.35	0.02	0.42	447	2130
Physical Appraisal	2.71 (<0.0001)	-0.005 (0.05)	-0.08 (<0.0001)	0.31	0.02	0.41	418	1744
Perceived health	2.74 (<0.0001)	-0.004 (0.28)	-0.07 (<0.0001)	0.29	0.03	0.39	210	1355
Depressed mood	1.96 (<0.0001)	0.0006 (0.83)		0.28	0.02	0.40	418	1808
Social support	2.51 (<0.0001)	-0.008 (0.12)	-0.13 (0.0005)	0.31	0.03	0.39	171	926
Role burden	2.78 (<0.0001)	-0.002 (0.42)	-0.19 (<0.0001)	0.32	0.02	0.41	418	1736

Predictor	Mean Values (p values)			Standard Deviations			Number	
	1 *	2 *	3 *	1 **	2 **	**	Women	Observations
Income adequacy	2.53 (<0.0001)	-0.001 (0.69)	-0.10 (<0.0001)	0.32	0.02	0.42	416	1631
Live Birth	2.18 (<0.0001)	-0.002 (.50)	0.04 (0.37)	0.33	0.02	0.42	418	1814
Employment	2.10 (<0.0001)	0.0004 (0.90)	0.14 (0.0001)	0.33	0.02	0.43	418	1814
History of sexual abuse	2.16 (<0.0001)	<-0.0001 (0.98)	0.11 (0.03)	0.32	0.02	0.42	238	1630

* 1, 2, 3 are the fixed effects (group averages) for the intercept, slope and covariate.

** 1, 2, 3 are the random effects (variability) for the intercept, slope and residual error.

Table 3

Final Random Effects Model for Perceived Stress with Age as Predictor and Other Significant Covariates Entered Simultaneously (N = 171; observations = 920)

	Coefficient (Betas)	Standard Error/ Standard Deviation	p value
<u>Fixed effects</u>			
₁ intercept	2.14	0.092	<0.0001
₂ Age (-47.9) years	<0.01	0.005	0.95
DepMood Depressed Mood	0.02	0.002	<0.0001
health Perceived Health	-0.04	0.010	<0.0001
Employ Employment	0.24	0.045	<0.0001
<u>Random effects</u>			
b ₁ Intercept ₁		0.27	
b ₂ Age (-47.9) years ₂		0.02	
b residual		0.37	