



Published in final edited form as:

*Stress Health*. 2011 August ; 27(3): e188–e194. doi:10.1002/smi.1360.

## Self-Reported Daily Stress, Squelching of Anger and the Management of Daily Stress and the Prevalence of Uterine Leiomyomata: The Ultrasound Screening Study

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### Abstract

Self-reported daily stress, ways of managing stress and squelching anger were examined in association with uterine leiomyomata (aka fibroids). These stress factors were obtained from 560 Black and 375 White women enrolled in the National Institute of Environmental Health Sciences Uterine Fibroid Study. Race-specific prevalence differences (PD) and 95% confidence intervals (95% CI) were calculated. Black women with severe stress had a prevalence of fibroids that was 11% higher (95% CI: 0%, 21%) than those in the no or mild stress group (referent). White women with severe stress, compared to the referent, had a non-significantly (NS) higher prevalence of fibroids [PD = 7%; 95% CI: (-103, 213)]. For both groups, moderate daily stress was associated with a weak elevation (NS) in fibroid prevalence. Black women who reported squelching their anger had an elevated prevalence of fibroids (8%) compared to non-squelchers [95% CI: (-03, 153)] while there was no association for White women. Women with symptomatic fibroids had higher stress than those without, but exclusion of symptomatic women only slightly attenuated the associations. Consistent with a previous report, symptomatic fibroids may cause stress. However, further research is warranted to prospectively investigate a possible aetiologic role for stress in the development of fibroids.

### Keywords

anger; stress; coping; leiomyoma; disparities

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## Introduction

Uterine leiomyomata (commonly called uterine fibroids) are benign smooth muscle tumors of clonal origin that are common in women of childbearing age (Stewart, 2001). For Black women, the risk of a clinical fibroid diagnosis is two to three times higher than that of White women, and estimated age-specific cumulative incidence based on ultrasound screening is significantly higher for Blacks than Whites after controlling for parity and body mass index (Baird & Dunson, 2003; Baird, Dunson, Hill, Cousins, & Schectman, 2003). Fibroids are hormonally dependent, developing after menarche and tending to regress after menopause (Cramer & Patel, 1990; Marshall et al., 1998). Black women develop fibroids at earlier ages than White women (Laughlin, Baird, Savitz, Herring, & Hartmann, 2009), and the cumulative risk of a hysterectomy for fibroids is 20% compared to 7% among White women between 25 and 45 years of age (Matchar et al., 2001).

This racial disparity in uterine fibroid prevalence and morbidity has not been sufficiently explained. Psychosocial stress may play a role. Stress can increase disease risks when stressful events are perceived as insurmountable and when coping strategies are unable to buffer the threat or demand (Cohen, Janicki-Deverts, & Miller, 2007). Studies have consistently reported that Blacks are more likely than Whites to suppress the expression of anger (Fleming & DuBois, 1981; Gentry, 1972; Johnson, 1989; Musante, Treiber, Davis, Waller, & Thompson, 1999; Steele, Elliot, & Phipps, 2003; Yarrow, 1958), and such suppression may be mediated by life strain (e.g. unemployment; Gentry, Chesney, Gary, Hall, & Harburg, 1982). The suppression of anger has been shown to be associated with increased resting blood pressure (Dimsdale et al., 1986) and higher rates of diagnosed breast cancer, lung cancer and rheumatoid arthritis (Broman & Johnson 1988; Johnson & Broman, 1987).

The arousal of the hypothalamic pituitary adrenal axis as a result of stress may influence the development of uterine fibroids through effects on adrenal glands and the production of gonadotrophins. Acute high stress can inhibit gonadotrophin secretion and reduce ovarian steroid production (Puder, Freda, Goland, Ferin & Wardlaw, 2000; Xiao, Xia-Zhang, & Ferin, 2000); thus, one might expect a protective effect. However, chronic stress can induce very different hormonal effects. In a study of Mayan women, higher daily urinary cortisol levels (indicative of chronic stress) predicted higher levels of gonadotrophins throughout the menstrual cycle and increased progesterin during the follicular phase (Nepomnaschy, Welch, McConnell, Strassmann, & England, 2004). This is consistent with experimental data in monkeys and research in humans showing that chronic lower-level stress (as opposed to higher acute stress) can promote luteinizing hormone (LH) secretion and adrenal progesterone production (Nepomnaschy et al., 2004; Xiao et al., 2000). Higher circulating LH has been linked to increased risk of fibroids (Baird, Kesner, & Dunson, 2006), and progesterone stimulates fibroid growth (Rein, Barbieri, & Friedman, 1995). We are suggesting that chronic stress-related increases in adrenal progesterone production and in pituitary LH secretion may be possible factors in a pathologic pathway.

To date, only one study has examined stress and fibroids. That study examined racial discrimination as a chronic stressor, and found that it was related to increased risk of fibroids in the Black Women's Health Study (Wise et al., 2007).

We examined perceived daily stress, squelching of anger and the management of daily stress as markers of chronic stress in association with the prevalence of uterine fibroids using cross-sectional data from 935 premenopausal Black and White women. We hypothesized that women who reported higher perceived daily stress, squelching anger and poor management of stress would have a higher prevalence of fibroids than those with low levels of these stress factors.

## Methods

The National Institute of Environmental Health Sciences Uterine Fibroid Study (UFS) enrolled women between 1996 and 1999 in the Washington, DC area in collaboration with the George Washington University Medical Center. The goal of the UFS was to estimate age-specific cumulative incidence of uterine fibroids and to assess risk factors for the condition. Detailed methods have been described previously (Baird et al., 2003). Briefly, the computerized membership records of a prepaid health plan in Washington, DC were used to randomly select women aged 35–49 years to participate in a telephone screener to determine study eligibility. Eligibility criteria were as follows: (1) the computerized listing had correctly identified a current member aged 35–49 years; and (2) a telephone interview could be conducted in English. Initial screening and enrollment resulted in 1,430 eligible participants with a response rate among those who screened eligible of about 80%. Of the 1243 premenopausal participants, the majority ( $n = 1143$ ) self-identified as belonging to either the Black or White non-Hispanic race group. Analyses were restricted to these two racial/ethnic groups. We excluded 149 women (13%) because they did not complete the self-administered questionnaire, the source of psychosocial stress measures. An additional 59 women were excluded because of missing data on fibroid status (no study ultrasound was completed or results were indeterminate). The final sample size for the analysis was 935 women. The Human Subjects Review Boards approved this study, and participants gave informed consent.

### Fibroid Status

Fibroid status at the time of study interview was determined based on pelvic ultrasound data: study ultrasound screening (76% of sample) or recent radiology record of pelvic ultrasound at clinic (21% of sample). 'Recent' was defined as within 5 years for an ultrasound showing fibroids and within 2 years for an ultrasound showing 'no fibroids'. Medical record review was conducted for women who had undergone a myomectomy. If neither the ultrasound nor medical record review could be conducted, self-report of a prior diagnosis of uterine fibroids was accepted. Self-report of 'no fibroids' was not accepted because undiagnosed fibroids were common (about half of the undiagnosed women in our study were found to have fibroids at ultrasound screening; Baird et al., 2003). Three percent of the sample had fibroid status based on self-report.

## Perceived Daily Stress and Stress Management Variables

Perceived daily stress was assessed using a self-administered single item question: ‘*Many people feel stressed in their day-to-day lives. How stressful is your day-to-day life?*’. Respondents indicated their level of perceived daily stress on a four-point scale (i.e. no stress, mildly stressful, moderately stressful and very stressful). Perceived daily stress was categorized as a three-level variable: low daily stress (i.e. none or mild daily stress levels, combined because less than 10% of white women reported no stress), moderate daily stress and high daily stress (i.e. severe). Low daily stress served as the referent category.

Respondents were also asked how they manage daily stress, ‘How do you deal with stress in your day to day life?’, with response choices: deals well with it; does not like it but manages; and feels anxious/overwhelmed/ exhausted. To assess anger suppression, respondents responded to the question, ‘How often do you feel the need to squelch or swallow strong feelings of anger?’ with ‘daily’, ‘weekly’ and ‘less often or never’ as the response choices. Both variables were originally three-level variables. However, sparse numbers in some cells led to convergence problems in models with white women. To remedy this problem and attain stable estimates, dichotomous variables were used. For management of stress—does not deal well (does not like it, but manages and feels anxious/overwhelmed/exhausted) was compared to deals well. For squelching anger, daily or weekly (squelching) were compared to less often or never (no squelching).

## Study Variables

Demographic and socio-economic characteristics came from either a telephone interview (age, occupation) or a self-administered questionnaire (education, income, marital status). The 2000 census occupational groupings (Fronczek & Johnson, 2003) was used to classify respondents into two occupational groups—white collar (e.g. professional/management positions) and non-white collar (e.g. service, labour, manufacturing positions)—based on self-report of longest held job. Total household income was adjusted based on the total number of people supported by the reported income and indexed to a household size of two. Adjusted household income was then categorized into four groups: <\$40,000 and/or receiving Medicaid; \$40,000–\$59,999; \$60,000–\$99,999; and \$100,000 or over.

## Statistical Analysis

All analyses were conducted separately by race group since the prevalence and risk factors for fibroids differ by race group, and the stress variables may have somewhat different meanings in the two groups. The associations between fibroid status and perceived daily stress, squelching anger and the management of stress were evaluated using Poisson regression with a robust variance estimator to estimate prevalence differences. The use of prevalence differences (PDs) provides a meaningful outcome measure because uterine fibroids are common (50% among White women and 74% among Black women).

Risk factors for fibroids were identified in prior analyses of the study data and included age at uterine fibroid assessment, body mass index, full-term pregnancies after age 24, age at menarche and physical activity. These were included *a priori* in the analyses as adjustment factors in one set of analyses (Baird & Dunson, 2003; Baird, Dunson, Hill, Cousins, &

Schectman, 2007). The associations between stress variables and prevalence of fibroids were tested with three adjustment sets: (1) age; (2) the *a priori* risk factors including age (3) the *a priori* risk factors plus socioeconomic status (SES) as reflected by education, occupational status and income. All covariates were included as ordinal variables. To begin to explore the direction of the association (stress causing fibroids versus fibroids causing stress), we examined the associations after excluding women who self-reported major fibroid symptoms (i.e. women who reported heavy gushing-type bleeding and severe cramping due to uterine fibroids, because their condition could be a source of daily stress. SAS version 9.1 was used to conduct the analyses (SAS Institute Inc., Cary, NC).

## Results

Table I shows the distribution of fibroid status, stress variables, fibroid risk factors and socioeconomic variables. Black and White women were about equally likely to report severe stress, but a higher proportion of White women reported moderate stress (Table I). When asked about the frequency of squelching anger, fewer White women reported squelching anger daily (Table I).

There was a significant association between fibroids and self-reported severe daily stress among the Black women (Table II). The prevalence of fibroids was 11% higher among Black women who reported severe daily stress [95% confidence interval (CI): 0%, 21%] than Black women who reported no or mild stress. This finding held after adjusting for fibroid risk factors and the combination of fibroid risk factors and SES. Excluding the Black women with self-reported major fibroid symptoms related to fibroids slightly attenuated the PD (9%) [Model 4: 95% CI: (-33, 223)]. Among White women, the age adjusted and the model with age and fibroid risk factors had PDs for severe daily stress and fibroids similar to those among the Black women, but the estimates did not reach statistical significance. There was further attenuation with adjustment for SES and after excluding White women with major fibroid symptoms.

In examining the association between squelching anger and fibroids, there was a modest association among the Black women, but none among the White women (Table III). Adjusting for age, Black women who reported squelching anger had a prevalence of fibroids that was 8% higher than those who did not squelch their anger (95% CI: 0%, 15%). For both Black and White women, the age adjusted prevalence difference for fibroids was similar (10% and 11%, respectively) comparing women who reported not dealing well with stress to women who reported dealing well with stress. However, the PD was only significant for the Black women.

## Discussion

Uterine fibroids are common in women of reproductive age, yet risk factors for this sometimes debilitating condition have received little study. We examined three single-item measures of psychosocial stress to evaluate associations with fibroids. We found support for the general hypothesis that chronic stress is associated with fibroids. Daily stress and the management of stress variables showed a generally similar association with fibroids in both

Blacks and Whites. However, although the speculated physiological pathways may be similar for White and Black women, we did find a different effect in terms of anger suppression. Frequent squelching of anger was associated with fibroids only for Blacks suggesting that this response may have different qualities of expression and health implications for Blacks compared to Whites.

We used an absolute measure, prevalence difference, in our presentation of the results. For conditions that are as prevalent as fibroids, a relative risk estimate will always be low to moderate (e.g., an exposure can never double the risk of a condition which occurs in more than half the unexposed), and the odds ratio does not approximate the relative risk. The prevalence difference accurately conveys the estimated public health impact of the exposure. Effect estimates such as those we report suggest a substantial public health impact when the baseline prevalence is as high as 50% or more as it may be for fibroids.

We examined chronic stress using single-item measures of stress that cannot fully capture the extent of stressful experiences. However, exposure misclassification is likely to be non-differential once women with major fibroid-related symptoms have been excluded. Thus, we can speculate that the associations we report are likely to be underestimates. More detailed stress assessment is needed.

Assessment of causality was not the intent of this paper. Rather, we were investigating cross-sectional associations to evaluate whether the findings support the possibility of an aetiologic role for stress. Fibroids that are symptomatic (i.e. causing bleeding and pain) can cause stress (Davis et al., 2009), and our data support this. However, when we excluded women who reported major fibroid symptoms, the associations were generally attenuated only slightly. This supports the theoretical arguments for chronic stress being aetiologically important and the need for prospective studies that measure stress before disease onset.

Given the racial disparities that exist in the prevalence of fibroids and the previous report from the Black Women's Health Study (Wise et al., 2007), research on Black women to explore race/ethnicity-related stressors may also help elucidate any role they might play in fibroid development.

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**Table I**

Distribution of uterine fibroid status, stress and socio-demographical characteristics of Black and White premenopausal women, NIEHS Uterine Fibroid Study, 1996–1999,  $n = 935$  \*

Characteristic	Black women ( $n = 560$ )		White women ( $n = 375$ )	
	n	%	n	%
Uterine fibroid status at interview				
Fibroids present	413	74	189	50
No fibroids	147	26	187	50
Daily stress				
None	69	12	8	2
Mild	259	46	154	41
Moderate	165	30	164	44
Severe	67	12	49	13
Squelching anger				
Less than weekly	290	52	221	59
Weekly	192	34	125	33
Daily	78	14	29	8
Management of stress				
Deals well	157	28	78	21
Does not like but manage	302	54	237	63
Feels anxious/overwhelmed/exhausted	96	17	58	16
Age at uterine fibroid diagnosis (years)				
<40	235	42	133	36
40–45	185	33	122	33
>45	140	25	120	32
Body mass index				
<25, normal	143	26	220	59
25–29, overweight	169	30	88	24
30, obese	247	44	67	18
Age at menarche (years)				
<11	64	12	15	4
11	87	16	56	15
12	150	27	97	26
13	134	24	130	35
14	54	10	44	12
>14	68	12	31	8
Full-term pregnancies after age 24				
0	280	50	235	63
1	175	31	55	15
2	105	19	85	23
Physical activity				
Low	208	37	99	27

Characteristic	Black women (n = 560)		White women (n = 375)	
	n	%	n	%
Medium	182	33	130	35
High	86	16	77	21
Very high	80	14	68	18
Educational attainment				
High school	117	21	12	3
Some/junior college	263	47	30	8
College degree/plus additional training	116	21	122	33
Post-graduate degree	64	11	211	56
Occupational status, longest held job				
White collar	200	36	286	76
Non-white collar	360	64	89	24
Total adjusted household income <sup>†</sup>				
<\$40,000	293	53	42	11
\$40,000–\$59,999	83	15	41	11
\$60,000–\$99,999	111	20	158	42
>\$100,000	64	12	132	35

\* Due to missing values, not all variables sum to 935.

<sup>†</sup> Income adjusted for household size and standardized to household size of 2.

Prevalence difference (PD) and 95% confidence interval (CI) for the association between self-reported daily stress and the presence of uterine fibroids, NIEHS Uterine Fibroid Study, *n* = 935

**Table II**

	n	None/mild			Moderate			Severe		
		PD	95% CI	PD	95% CI	PD	95% CI			
<b>Blacks</b>										
Model 1 <sup>*</sup>	560	Referent	0.05	-0.03, 0.14	0.11	0.00, 0.21				
Model 2 <sup>†</sup>	553	Referent	0.03	-0.05, 0.12	0.11	0.01, 0.22				
Model 3 <sup>‡</sup>	544	Referent	0.04	-0.04, 0.13	0.11	0.00, 0.22				
Model 4 <sup>§</sup>	487	Referent	0.03	-0.07, 0.12	0.09	-0.03, 0.22				
<b>Whites</b>										
Model 1 <sup>*</sup>	375	Referent	0.09	-0.02, 0.19	0.13	-0.03, 0.29				
Model 2 <sup>†</sup>	372	Referent	0.07	-0.04, 0.18	0.10	-0.07, 0.26				
Model 3 <sup>‡</sup>	370	Referent	0.07	-0.04, 0.18	0.07	-0.10, 0.24				
Model 4 <sup>§</sup>	355	Referent	0.08	-0.03, 0.20	0.06	-0.11, 0.23				

<sup>\*</sup> Model 1: age-adjusted.

<sup>†</sup> Model 2: adjustment for age, BMI, parity, age at menarche and physical activity.

<sup>‡</sup> Model 3: adjustment for all model 2 variables plus education, occupational status and adjusted household income.

<sup>§</sup> Model 4: adjustment for all model 2 variables with the exclusion of women with self-reported major fibroid symptoms.

Prevalence difference (PD) and 95% confidence interval (CI) for the association of self-reported squelching of anger and management of stress with the presence of uterine fibroids, NIEHS Uterine Fibroid Study, *n* = 935

**Table III**

	Squelching of anger				Stress management				
	Less often or never		Daily or weekly		Deals well		Does not deal well		
	n	PD	95% CI	n	PD	95% CI	n	PD	95% CI
<b>Blacks</b>									
Model 1 <sup>*</sup>	560	Referent	0.08	0.00, 0.15	555	Referent	0.10	0.00, 0.20	
Model 2 <sup>†</sup>	553	Referent	0.07	-0.01, 0.14	548	Referent	0.09	-0.01, 0.19	
Model 3 <sup>‡</sup>	544	Referent	0.07	-0.01, 0.15	539	Referent	0.09	-0.01, 0.19	
Model 4 <sup>§</sup>	487	Referent	0.07	-0.01, 0.15	483	Referent	0.07	-0.04, 0.18	
<b>Whites</b>									
Model 1 <sup>*</sup>	375	Referent	-0.04	-0.14, 0.06	373	Referent	0.11	-0.08, 0.31	
Model 2 <sup>†</sup>	372	Referent	-0.02	-0.13, 0.08	370	Referent	0.05	-0.15, 0.25	
Model 3 <sup>‡</sup>	370	Referent	-0.04	-0.14, 0.07	368	Referent	0.04	-0.16, 0.23	
Model 4 <sup>§</sup>	355	Referent	-0.05	-0.15, 0.06	353	Referent	0.05	-0.17, 0.26	

<sup>\*</sup> Model 1: age-adjusted.

<sup>†</sup> Model 2: adjustment for age, BMI, parity, age at menarche and physical activity.

<sup>‡</sup> Model 3: adjustment for all model 2 variables plus education, occupational status and adjusted household income.

<sup>§</sup> Model 4: adjustment for all model 2 variables with the exclusion of women with self-reported major fibroid symptoms.