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Self-reported Abuse in Childhood and Risk of Uterine Leiomyoma: The Role of Emotional Support in Biological Resiliency

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Abstract

Background—Childhood adversities are associated with adult health. We hypothesize that exposure to physical and sexual abuse in childhood and adolescence will be associated with incidence of clinically symptomatic uterine leiomyomas (fibroids) through influences on health behaviors and reproductive hormone regulation.

Methods—Participants included 68,505 women enrolled in the Nurses' Health Study II, an ongoing prospective cohort study of premenopausal women from 14 US states aged 25– 42 years at enrollment (1989), who completed a retrospective questionnaire on childhood violence exposure (2001). A cumulative indicator of severity and chronicity of child/teen violence exposure was derived using factor analysis. We used a Cox proportional-hazards model to estimate the incidence rate ratios (IRRs) and 95% confidence intervals (CIs).

Results—During the 728,865 woman-years of follow-up (1989–2005), 9,823 incident diagnoses of ultrasound- or hysterectomy-confirmed uterine leiomyomas were reported; 65% reported any physical or sexual abuse. A dose-response association between cumulative abuse and fibroid risk was found. Compared with those who reported no abuse, multivariable IRRs for ultrasound or hysterectomy-confirmed uterine leiomyomas were 1.08 (95% CI= 1.03–1.13), 1.17 (1.10–1.24), 1.23 (1.14–1.33), 1.24 (1.10–1.43), and 1.36 (1.18–1.54), for cumulative exposures ranging from mildest to most severe. Increased emotional support in childhood also attenuated associations.

Conclusion—Severity and chronicity of child/teen sexual and physical abuse was associated with increasing risk of clinically-detected fibroids among premenopausal women.

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Uterine leiomyomas, also known as fibroids or myomas, are benign, hormone-dependent tumors that are clinically symptomatic in 20%–25% of reproductive age women.[1] Despite being the most common pelvic neoplasm in women of reproductive age,[1] the etiology of myomas is poorly understood. Established risk factors for fibroids include age,[2] African American ethnicity,[3] and family history.[4] Body mass index (BMI) has been associated with increased fibroid risk in several studies, with the highest risk among overweight women,[5, 6] although this is not always the case.[7, 8] Ovarian hormone regulation is thought to play a central role.[9] The incidence and clinical progression of fibroids is associated with younger age at menarche,[10, 11] infertility,[10] and lower parity.[12] Age at menarche has been associated with elevated weight gain in early life.[13]

A growing body of evidence indicates an association between early life social adversities and adult health. Physical, sexual, and emotional abuse in childhood has been associated with increased mortality and morbidity in adulthood, and poor health behaviors.[14] The "allostatic load" hypothesis postulates that chronic social stressors may adversely affect the physiological systems responsible for maintaining homeostasis and thereby negatively influence health over time.[15] Research in animal and human models demonstrates that severe stress in early life is associated with altered regulation of the hypothalamic pituitary-adrenal axis and autonomic stress response that persists even into adulthood.[16] Chronic psychological stressors contribute to functional changes in neural, endocrine, and immune processes, as well as emotional and behavioral responses.[17, 18] Population-based studies have demonstrated a relation between physical and sexual abuse in childhood and both earlier age at menarche[19, 20] and elevated BMI and obesity[21]—factors which are also associated with fibroid risk.[8] However, the impact of child abuse on fibroid risk has not been investigated.

Although the etiology of uterine leiomyomas is not completely understood, overproduction and accumulation of extracellular matrix and resulting fibrous tissue development are hallmark features.[22] Evidence exists that this pathogenesis is influenced by hemodynamic stress, pro-inflammatory cytokines, impaired repair of injured tissue, and hormonal dysregulation including hyperinsulinemia, gluccocorticoid stimulation[22–24]—processes that may be vulnerable to stress-elicited disruptions.[17]

While studies document associations between exposure to violence and gynecologic health —including dysmenorrhea, sexually transmitted infections, and chronic pelvic pain— findings are mixed.[25, 26] One cross-sectional survey found a significant association between intimate partner violence and hysterectomy,[26] but a case-control study exploring multiple health outcomes did not find an association between such violence and fibroids.[27] These studies of small clinic-based samples are limited in statistical power and generalizability.

Provision of emotionally supportive relationships with parents or caretakers is associated with children's enhanced problem solving, emotion regulation, mental health, and fewer health risk behaviors.[28, 29] Moreover, research indicates that parental emotional support is protective against the potential negative impacts of victimization on health and development.[28] Several studies have established a link between limited social support, insecure attachment, and hypothalamic pituitary-adrenal axis dysregulation.[30] Emotional

support may enhance biological resiliency in the face of childhood adversities and thereby buffer the impact of chronic psychological stress and modify risk for fibroids.

The aims of this study were to examine relationships between physical and sexual abuse occurring in childhood or adolescence and risk for uterine fibroids in adulthood. We hypothesized that the chronicity and severity of abuse in early life would have a graded association with fibroid risk in adult women. We also hypothesized that positive emotional support in childhood would buffer the impact of abuse on fibroid risk. Uniquely, this study uses a national sample of premenopausal women from throughout the United States.

METHODS

Study Population

The sample was recruited from the Nurse's Health Study II, an ongoing prospective cohort study designed to explore factors that influence morbidity and mortality among women. This study began in September of 1989 with a sample of 116,678 registered female nurses aged 25–44 years, from 14 U.S. states. Respondents have been contacted biennially with questionnaires regarding health behaviors and disease occurrence. Follow-up of the cohort is greater than 90%.

A supplemental questionnaire on lifetime exposure to violence victimization was administered in 2001 to 91,248 study participants (excluding those who had previously requested short form surveys or who had required more than four mailings before responding to the 1999 questionnaire). Non-respondents received a reminder postcard. We received 68,505 questionnaires, a 75% response rate. The survey obtained separate approval by the Institutional Review Board at Brigham and Women's Hospital and the Human Subjects Committee at Harvard School of Public Health as a sub-study of Nurse's Health Study II protocol. Completion of the supplemental questionnaire indicated their consent to participate.

The study population for this analysis was restricted to women who were premenopausal, with intact uteri in 1989 and who responded to the 2001 violence survey. Women were excluded if they had the following conditions: history of leiomyoma prior to September 1989 (n = 3406), unknown date of leiomyoma diagnosis (n = 65), reported diagnosis of any cancer other than nonmelonoma skin cancer (n = 591), were postmenopausal (n = 1315), had a hysterectomy (n = 1700), had no information on exposure to violence during childhood (n = 463) or childhood emotional support (n = 18), or unclear menopausal status (n = 332). After the exclusions, 60,615 women remained for analysis.

Measures

Assessment of the outcome—Leiomyoma was self-reported as "ever uterine fibroids (yes/no)," with indication of the method of confirmation (pelvic exam, ultrasound or hysterectomy), on each biennial questionnaire since 1993; the interval date of diagnosis was also ascertained on the 1993 survey (before 9/89, 9/89-5/91, 6/91-5/93, 6/93 or later). The diagnosis date was set to the midpoint of the reported diagnosis interval for closed interval periods. For prospectively open-ended intervals, the date was assigned to the midpoint of the

interval start and the questionnaire return date. For retrospectively open-ended intervals, the date of diagnosis was set to the end date of the interval. Therefore, we are measuring the incidence of first diagnosis by ultrasound or hysterectomy, rather than incidence of onset of fibroid tumor, which cannot be ascertained. Time at risk was defined as the number of months between the return of the 1989 questionnaire and May 2005, death, onset of menopause, diagnosis of cancer, or date of fibroid diagnosis (whichever came first). Women who reported a new diagnosis confirmed by pelvic exam alone were not allowed to contribute person-time during the reported interval but were allowed to reenter the analysis at a later date if they had a hysterectomy or ultrasound confirmation. If a participant reported both a hysterectomy and a fibroid diagnosis confirmed by ultrasound or hysterectomy in the same time interval, the diagnosis was further classified as hysterectomy-confirmed.

Marshall and colleagues approached 243 NHS II participants who reported fibroids on the 1993 questionnaire (100 white and 143 black women) to participate in a validation study. Among the 130 women who released their medical records, 116 records were obtained and the self-report was confirmed by medical records in 108 (92% of black and 94% of white participants).[31]

Assessment of childhood and adolescent exposure to violence—Childhood and adolescent exposures to abuse were measured using items from the Childhood Trauma Questionnaire-short form,[32] the Revised Conflict Tactics Scale,[33] and the Sexual Experience Survey.[34] Adult emotional, physical and sexual abuse by an intimate partner was measured using questions adapted from the McFarlane Abuse Assessment Screen.[35]

Childhood Trauma Questionnaire: Exposure to physical, emotional, and verbal abuse in childhood (prior to age 11) was assessed using items from the Childhood Trauma Questionnaire-short form.[32] We included a 3-item subscale on physical abuse (e.g., “People in my family hit me so hard that it left me with bruises and marks,” “The punishments I received seemed cruel,” and “I was punished with a belt, a board, a cord, or some other hard object”) and two items on emotional abuse (e.g., “People in my family said hurtful or insulting things to me” and “yelled and screamed at me”). A single item was included to assess social support, “There was someone in my family who helped me feel that I was important or special.” All items are rated on a 5-point Likert scale according to frequency (1 = never, 2 = rarely, 3 = sometimes, 4 = often, or 5 = very often), and a total score was derived by summing across items. The internal consistency/reliability of the summed Child Trauma Questionnaire score was high (Cronbach’s alpha=0.88), excluding the theoretically distinct question on emotional support. The Child Trauma Questionnaire score was modeled as quartiles, and emotional support was explored independently as a dichotomous (very often/often and sometimes/rarely/never) variable.

Sexual and Physical Abuse: Five items from the Revised Conflict Tactics Scale instrument were used to assess exposure to physical abuse by a parent, step-parent or adult guardian.[33] Respondents were queried about specific types of abuse for childhood (prior to age 11) and adolescence (11–17 years), including: physical attack, choke or burn, kick bite or punch, push or grab, and being hit with something that hurt; the frequency of each type of abuse was indicated on a 4 point scale (never, once, a few times, more than a few times).

Questions on forced sexual experiences were modified from questions on the Sexual Experiences Survey.[34] Participants rated the frequency of the following exposures on a 3-point scale (never, once, more than once): “were you ever touched in a sexual way” or “forced into any sexual activity” by an adult or an older child, separately for childhood and adolescence. Subjects also reported whether their parent(s) or guardians spanked them for discipline (up to age 11).

In order to capture a latent construct—cumulative violence exposure, which incorporates both chronicity and severity—we utilized a principle components factor analysis methodology with oblique (promax) rotation (eTable 1, http://links.lww.com). We collapsed the highest exposure categories for physical violence into a single category so all variables had only 3 possible responses. The number of components retained was based on scree plots, and, using the Kaiser criteria, we retained all factors with an eigenvalue >1.[36] Items with factor loadings > 0.45 were assigned to the factor for which they had the greatest loading. This resulted in a two-factor solution representing the domains of physical and sexual abuse. Internal consistency/reliability for each of the abuse factors was determined by Cronbach’s alpha, and all factors were adequate (≥0.70). The item related to spanking for discipline did not load on either of the abuse factors. Next, we evaluated the population frequency distribution of each type of violence and number of events of each type of violence within the two factors separately. Categories that classify violence exposure by severity and chronicity were based on the factor analysis and frequency trends within each factor (see eTable 2, http://links.lww.com).

Statistical Analyses

Descriptive analyses were conducted to explore the relationship between the demographic variables and violence exposure categories, using frequency distributions for categorical and t-tests for continuous variables. In all analyses the referent group includes those who reported no violence in childhood or adolescence. Those who reported only exposure to spanking for discipline were included in the referent group, because spanking was considered to be theoretically and empirically (as measured by the factor analysis) distinct from abuse.

Person-months of follow-up were counted from the date of return of the 1989 questionnaire until the date of return of the 2005 questionnaire. Person-months of follow-up were assigned to groups according to baseline exposure status. The incidence rates of fibroids, confirmed by ultrasound or hysterectomy, for specific violence exposure categories were computed by dividing the number of events by the person-time at risk in that category.

Multivariable Cox proportional hazards regression models with time-varying covariates (including age, BMI, age at first birth, parity) were used to estimate incidence rate ratios while controlling for multiple risk factors using the SAS PROC PHREG procedure (SAS Institute, 1991). All analyses controlled for confounders, including: age (months), time period (months), race/ethnicity (Asian, Black, Latina, White, Other), and socioeconomic status in childhood (SES). Childhood SES was available for a subset of our sample, as 30,562 mothers of NHS II participants who were included in these analyses had participated in the 2001 Maternal Cohort Study and responded to a mailed questionnaire that ascertained

information on educational level of mother and father. We modeled highest parental educational attainment at participants' birth as a trichotomous variable—less than a high school diploma, high school diploma, advanced education. Known risk factors for leiomyoma, that were also previously associated with childhood violence, were explored as mediators including: parity (1, 2, ≥3 pregnancies of >6 months' duration); age of menarche (≤10, 11, 12, 13, 14,15,16, ≥17 years of age); age of first oral contraceptive use (never, 13–16, 17–20, 21–24 years); BMI (continuous measure in kg/m^2); diastolic blood pressure (continuous measure in mm Hg); age of first birth (≤22, 23–25, ≥25 years); time since last birth (1–7, 8–15, ≥16 years); age of first oral contraceptive use (never, 13–16, 17–20, 21–24, ≥25 years); history of infertility(yes, no); menstrual irregularity (regular, somewhat irregular or 21–30 day cycle, very irregular >40 day cycle). Indicators were used to model those with missing information. We repeated analyses excluding all those with incomplete information on covariates, with the exception of parental education because this variable was available only for a subset of our cohort, and we found no appreciable difference in effect estimates. We also repeated analyses including an indicator for routine gynecological surveillance—annual breast or pelvic exam (assessed as: no, yes for screening, yes for symptoms, missing)—dichotomized as annual screening yes/no.

RESULTS

Frequencies of childhood and adolescence abuse exposures are reported in Table 1. Overall, 65% of women in the cohort reported one or more abuse exposures during childhood or adolescence, and 48% reported abuse that started in childhood (up to age 11). Specifically, 53% (n = 32,054) reported child/teen physical abuse and 33% (n = 19,854) reported child/teen sexual abuse (22% reported inappropriate sexual touching only, and 11% reported forced sexual activity). Approximately 21% of the cohort experienced both physical and sexual abuse prior to adulthood.

Table 2 demonstrates the age-adjusted distribution of potential leiomyoma risk factors by exposure to violence. Several potential risk factors for leiomyomas were at least modestly increased among women who had experienced abuse; these included higher BMI, blood pressure, and risk of hypertension, as well as younger age at menarche (≤11 years) and first birth (≤24 years). Women with a history of abuse were also more likely to have used oral contraceptives before age 17 years.

During the 728,826 woman-years of follow-up, 9823 incident cases of uterine leiomyomata confirmed by ultrasound or hysterectomy were reported. In comparison with those who reported no history of exposure to violence in childhood or adolescence, the IRR for the four measures of childhood abuse exposure were greater than 1.0. Both physical and sexual abuse history were positively associated with a higher incidence of uterine leiomyomas. A graded association between cumulative abuse exposure and adjusted IRR of leiomyoma was demonstrated (Table 3). Those exposed to severe chronic and multiple types of abuse had a higher incidence of leiomyoma (multivariable IRR = 1.36 [95% CI = 1.18–1.56]), Results were similar when we repeated our analyses using the Child Trauma Questionnaire score for childhood abuse and using the physical and sexual violence severity measure (Table 3).

Having a consistent (very often or always) emotionally supportive relationship in childhood was protective when included as a covariate in our multivariate model of cumulative violence predicting leiomyoma (IRR = 0.95 [0.91–1.00]). In stratified analyses, a similar dose-response pattern between cumulative early life violence and risk of incident fibroids was present among those with and without positive support in childhood (eTable 3, http://links.lww.com). However, among those exposed to multiple forms of severe abuse as a child/teen, the IRR was 1.70 (1.32–2.18) among those without an emotionally supportive relationship in childhood in comparison to those with positive support (1.24 [1.03–1.50]). This finding was replicated with the measures of abuse severity and type (eTable 3, http://links.lww.com). There was little statistical evidence of heterogeneity between the high and low emotional support groups (test for interaction, $P = 0.25$) or between type of abuse and cumulative abuse (test for interaction, $P = 0.44$), based on Cochrane's Chi-Square test. Finally, violence in adulthood was not associated with leiomyomas among those who were not exposed to abuse in childhood or adolescence (0.98 [0.84–1.14]), but was modestly associated with fibroids among those exposed to childhood abuse (1.08 [1.04–1.14]). Nonetheless, formal assessment of heterogeneity does not provide evidence that these estimates are statistically distinct (test for interaction, $P = 0.24$). We did an analysis among the subset of the population who had not had a diagnosis of fibroids at the time of the violence questionnaire (2001) to investigate fibroid risk prospectively and found a similar graded association with violence severity and chronicity (eTable 4, http://links.lww.com).

We also performed sensitivity analyses to assess the impact of seeking medical care on the relation between child abuse and leiomyoma risk. We found no attenuation of the impact of early life violence on risk for incident myomas when controlling for history of annual breast or pelvic exams (results not shown), although history of annual breast or pelvic exam was a predictor of leiomyoma diagnosis (1.17 [1.08–1.26]). We also restricted our sample to those reporting having had a pelvic exam and found no difference in our results.

DISCUSSION

Our analyses show a graded association between early-life exposure to physical, sexual, and emotional abuse and leiomyoma risk. Moreover, cumulative exposure, severity of abuse, and duration of exposure were all associated with leiomyoma risk in a dose-response pattern. The relation was only modestly attenuated by adjustment for a number of confounders as well as putative intermediate variables, including age of menarche, age of first birth, age of first oral contraceptive use, BMI, and diastolic blood pressure. Having an emotionally supportive relationship in childhood further modified the strength of the association between child/teen abuse and leiomyoma risk.

Guided by the allostatic-load model, which postulates that chronic stress affects physiological systems that maintain homeostasis,[15] a number of plausible pathways through which exposure to violence may influence fibroid risk have been posited. First, chronic violence may alter hypothalamic-pituitary-adrenal and -gonadal axes functioning, thereby influencing bioavailability of estrogens and increasing risk for fibroid development. Experiences of violence have been associated with earlier onset of puberty,[20, 37] altered hypothalamic-pituitary axis function in young women,[16, 38, 39] and earlier onset of

perimenopause in older women.[40] Animal and human studies have documented an association between deficient nurturing and hypothalamic-pituitary dysregulation. [30, 41, 42] Consistent with prior studies, women in this sample who experienced violence had earlier menarche[20, 37] and age of first pregnancy[43, 44]—both factors that are also associated with fibroid risk.[45] Adjustment for these variables modestly attenuated the associations between abuse and fibroid risk. It is plausible that exposure to violence in early life may affect fibroid risk in part by influencing ovarian function

Elevated systolic and diastolic blood pressure has been associated with fibroid risk in this cohort and others.[24, 46] Empirical evidence from cross-sectional studies demonstrates an association between stress and increased blood pressure.[47] In this cohort, self-reported blood pressure and physician-diagnosed hypertension were higher among women reporting a history of childhood or adolescent abuse,[48] and inconsistent findings have been revealed among those with intimate partner violence.[26, 27] In our analysis, adjustment for blood pressure somewhat dampened the association of abuse with fibroids. Future investigation is needed to more definitively explore this as a potential mechanism.

Another potential pathway between violence and fibroid risk may be via elevated BMI. Exposure to violence in childhood has been linked to BMI, obesity,[14, 21] and disordered eating patterns.[49, 50] We also found higher adult BMI among women with abuse histories. Although findings are mixed, some epidemiologic studies have demonstrated an association between BMI and fibroid risk.[5–7] Insulin has been shown to stimulate leiomyoma cell growth in tissue culture[51] and promote cellular mitosis,[52] and may directly increase fibroid risk, although findings in cohort and case-control studies are mixed.[53–55] Alternatively, insulin may indirectly elevate risk through its impact on the sympathetic nervous system, increasing vascular tone and elevating blood pressure, or by increasing circulation of ovarian hormones (estrogen) by stimulating insulin receptors or endothelial growth factors. However, in our study, adjustment for BMI and blood pressure only slightly attenuated the association between abuse and risk of fibroids by 3% in the highest cumulative abuse category.

Women with a history of violence exposure may be more likely to utilize medical care or seek more intensive investigation of medical problems.[25, 56] Annual breast or pelvic exam may be an intermediate variable (a proxy measure of gynecologic health surveillance). While there is evidence that abuse history is associated with chronic pelvic pain[57] and may indeed elevate gynecologic screening, there is also evidence that those with a history of abuse, particularly sexual abuse, may have difficulty with pelvic examinations and be reluctant to undergo screening.[58] If so, then differential detection of fibroids by ultrasound or hysterectomy may occur. However, when controlling for annual breast or pelvic exam in the multivariate model, the relation between exposure to violence and fibroid risk was not attenuated.

Research evidence suggests that supportive relationships are protective against the potential negative impacts of victimization on health and development.[59] Our results support a general trend of a supportive relationship in childhood buffering the impact of abuse on fibroid risk in adulthood.

There are also important limitations. The study is based on retrospective report of violence exposure. Notably, our sensitivity analysis of incident cases post-violence exposure report yielded similar results. Survivors of childhood abuse may be less able to recall traumatic events accurately,[60] or may be more likely to report inaccurately due to social pressures.[61] However, self-report measures of child maltreatment have demonstrated strong validity.[61] If present in our sample, such under-reporting is most likely to have caused underestimation of the association between abuse and fibroids. On the other hand, if women with fibroids are more likely to recall more negative childhood experiences, or appraise early childhood events as abusive, then we might have over-estimated associations of abuse with fibroid risk. However, it seems unlikely that presence of fibroids would affect recall or appraisal of abuse to any meaningful extent. Use of the Child Trauma Questionnaire which asks about discrete and objective events (rather than one's perception of having been abused) is less prone to inaccurate recall.[62] Additionally, the reported rates of child abuse exposure are consistent with rates reported in national surveys and with retrospective self-report of childhood violence in adulthood.[63, 64]

It is also possible that early-life violence is correlated with other unmeasured factors related to reproductive health in adulthood. Hypothetically, early development of secondary sexual characteristics—which may increase fibroid risk through enhanced sex hormone exposure—may be associated with risk for childhood sexual abuse.[65] Also, childhood adversities tend to co-occur.[14] Children in families with neglect, parental substance abuse, marital violence, and housing insecurity are also more likely to experience victimization in childhood.[66] Chronicity, duration, and frequency of sexual abuse has been associated with multiple forms of household dysfunction and neglect in a graded fashion.[66] Lower childhood SES is associated with heightened risk for abuse[67] and poor health outcomes,[68] although our analyses control for parental education. Social stressors have been associated with timing of sexual maturation.[19] Therefore if early life abuse is associated with other childhood adversities the association between violence and fibroids may be driven by cumulative impact of social stressors.

In summary, exposure to physical, sexual, or emotional abuse in childhood and adolescence was associated with an increased risk for clinically symptomatic fibroid tumors in adulthood. The impact of early life adversity on fibroid risk persisted even among those with no future violence exposure in adulthood. Early life exposure to violence may underpin biological and behavioral patterns that affect fibroid risk in adulthood. While our study is partially prospective, a prospective study with repeated measures of violence and screening for fibroids may yield a more comprehensive view of how the biological and behavioral consequences of social stress contribute to the etiology, prevalence, or clinical severity of this far-too-common condition.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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References

1. Newbold RR, DiAugustine RP, Risinger JI, et al. Advances in uterine leiomyoma research: conference overview, summary, and future research recommendations. Environ Health Perspect. 2000; 108(Suppl 5):769–773. [PubMed: 11035980]
2. Marshall LM, Spiegelman D, Barbieri R, Goldman M, Manson J, Colditz G, Willett W, Hunter D. Variation in the incidence of uterine leiomyoma among premenopausal women by age and race. Obstet Gynecol. 1997; 90:967–973. [PubMed: 9397113]
3. Day Baird D, Dunson DB, Hill MC, Cousins D, Schectman JM. High cumulative incidence of uterine leiomyoma in black and white women: ultrasound evidence. Am J Obstet Gynecol. Jan; 2003 188(1):100–107. [PubMed: 12548202]
4. Luoto R, Kaprio J, Rutanen EM, Taipale P, Perola M, Koskenvuo M. Heritability and risk factors of uterine fibroids--the Finnish Twin Cohort study. Maturitas. 2000; 37(1):15–26. [PubMed: 11099869]
5. Terry KL, De Vivo I, Hankinson SE, Spiegelman D, Wise LA, Missmer SA. Anthropometric characteristics and risk of uterine leiomyoma. Epidemiology. Nov; 2007 18(6):758–763. [PubMed: 17917603]
6. Wise LA, Palmer JR, Spiegelman D, et al. Influence of body size and body fat distribution on risk of uterine leiomyomata in U.S. black women. Epidemiology. May; 2005 16(3):346–354. [PubMed: 15824551]
7. Baird DD, Dunson DB, Hill MC, Cousins D, Schectman JM. Association of physical activity with development of uterine leiomyoma. Am J Epidemiol. Jan 15; 2007 165(2):157–163. [PubMed: 17090618]
8. Schwartz SM. Epidemiology of uterine leiomyomata. Clinical Obstetrics and Gynecology. 2001; 44(2):316–326. [PubMed: 11344995]
9. Robboy SJ, Bentley RC, Butnor K, Anderson MC. Pathology and pathophysiology of uterine smooth-muscle tumors. Environ Health Perspect. 2000; 108(Supplement 5):779–784. [PubMed: 11035982]
10. Marshall LM, Spiegelman D, Goldman M, Manson J, Colditz G, Barbieri R, Stampfer M, Hunter D. A prospective study of reproductive factors and oral contraceptive use in relation to the risk of uterine leiomyomata. Fertility and Sterility. 1998; 70:432–439. [PubMed: 9757871]
11. Sato F, Miyake H, Nishi M, Mori M, Kudo R. Early normal menstrual cycle pattern and the development of uterine leiomyomas. J Womens Health Gend Based Med. 2000; 9(3):299–302. [PubMed: 10787225]
12. Baird DD, Dunson DB. Why is parity protective for uterine fibroids? Epidemiology. Mar; 2003 14(2):247–250. [PubMed: 12606893]
13. Sloboda DM, Hart R, Doherty DA, Pennell CE, Hickey M. Age at menarche: Influences of prenatal and postnatal growth. J Clin Endocrinol Metab. Jan; 2007 92(1):46–50. [PubMed: 17062767]
14. Felitti VJ, Anda RF, Nordenberg D, et al. Relationship of childhood abuse and household dysfunction to many of the leading causes of death in adults. The Adverse Childhood Experiences (ACE) Study. Am J Prev Med. 1998; 14(4):245–258. [PubMed: 9635069]
15. McEwen B. Protective and damaging effects of stress mediators. New England Journal of Medicine. 1998; 338(3):171–179. [PubMed: 9428819]
16. Heim C, Newport DJ, Heit S, et al. Pituitary-adrenal and autonomic responses to stress in women after sexual and physical abuse in childhood. Jama. 2000; 284(5):592–597. [PubMed: 10918705]

17. Miller G, Chen E, Cole SW. Health psychology: developing biologically plausible models linking the social world and physical health. Annu Rev Psychol. 2009; 60:501–524. [PubMed: 19035829]
18. Nemeroff C. Neurobiological consequences of childhood trauma. J Clin Psychiatry. 2004; 65(Suppl 1):18–28. [PubMed: 14728093]
19. Romans S, Martin JM, Gendall K, Herbison GP. Age of menarche: the role of some psychosocial factors. Psychol Med. 2003; 33(5):933–939. [PubMed: 12877408]
20. Wise LA, Palmer JR, Rothman EF, Rosenberg L. Childhood abuse and early menarche: findings from the black women's health study. Am J Public Health. Oct; 2009 99 (Suppl 2):S460–466. [PubMed: 19443822]
21. Williamson DF, Thompson TJ, Anda RF, Dietz WH, Felitti V. Body weight and obesity in adults and self-reported abuse in childhood. Int J Obes Relat Metab Disord. 2002; 26(8):1075–1082. [PubMed: 12119573]
22. Sozen I, Arici A. Interactions of cytokines, growth factors, and the extracellular matrix in the cellular biology of uterine leiomyomata. Fertil Steril. Jul; 2002 78(1):1–12. [PubMed: 12095482]
23. Arici A, Sozen I. Expression, menstrual cycle-dependent activation, and bimodal mitogenic effect of transforming growth factor-beta1 in human myometrium and leiomyoma. Am J Obstet Gynecol. Jan; 2003 188(1):76–83. [PubMed: 12548199]
24. Boynton-Jarrett R, Rich-Edwards J, Malspeis S, Missmer SA, Wright R. A prospective study of hypertension and risk of uterine leiomyomata. Am J Epidemiol. Apr 1; 2005 161(7):628–638. [PubMed: 15781952]
25. Campbell JC. Health consequences of intimate partner violence. Lancet. 2002; 359:1331–1336. [PubMed: 11965295]
26. Coker AL, Smth PH, Bethea L, King MR, McKeown RE. Physical health consequences of physical and psychological intimate partner violence. Arch Fam Med. 2000; 9:451–457. [PubMed: 10810951]
27. Campbell J, Jones AS, Dienemann J, Kub J, Schollenberger J, O'Campo P, Carlson Gielen A, Wynne C. Intimate partner violence and physical health consequences. Arch Intern Med. 2002; 162:1157–1163. [PubMed: 12020187]
28. Cohen S, Wills TA. Stress, social support, and the buffering hypothesis. Psychol Bull. Sep; 1985 98(2):310–357. [PubMed: 3901065]
29. Thoits PA. Social support as coping assistance. J Consult Clin Psychol. Aug; 1986 54(4):416–423. [PubMed: 3745593]
30. Meany MJ, Aitken DH, van Berkel CH, Bhatnagger S, Sapolsky RM. Effect of neonatal handling on age-related impairments associated with the hippocampus. Science. 1988; 239:766–768. [PubMed: 3340858]
31. Marshall LMSD, Barbieri R, Goldman M, Manson J, Colditz G, Willett W, Hunter D. Variation in the indidence of uterine leiomyoma among premenopausal women by age and race. Obstet Gynecol. 1997; 90:967–973. [PubMed: 9397113]
32. Bernstein D, Fink L, Handelsman L, Foote J, Lovejoy M, Wenzel K, Sapareto E, Ruggiero J. Initial reliability and validity of a new retrospective measure of child abuse and neglect. Am J Psychiatry. 1994; 151:1132–1136. [PubMed: 8037246]
33. Straus M, Hamby SL, Boney-McCoy S, Sugarman DB. The revised conflict tactics scales (CTS2). Journal of Family Issues. 1995; 17(3):283–316.
34. Koss MP, Oros CJ. Sexual experience survey. J Consult Clin Psychol. 1982; 50:455–457. [PubMed: 7096751]
35. McFarlane J, Parker B, Soeken K, Bullock L. Assessing for abuse during pregnancy. Severity and frequency of injuries and associated entry into prenatal care. JAMA. 1992; 267(23):3176–3178. [PubMed: 1593739]
36. Hactcher, L. A step-by-step approach to using SAS for factor analysis and structural equation modeling. Cary, NC: SAS Institute, Inc; 1994.
37. Zabin LS, Emerson MR, Rowland DL. Childhood sexual abuse and early menarche: the direction of their relationship and its implications. J Adolesc Health. May; 2005 36(5):393–400. [PubMed: 15837343]

38. De Bellis MD. Abuse and ACTH response to corticotropin-releasing factor. Am J Psychiatry. 2002; 159(1):157–158. [PubMed: 11772726]
39. Heim C, Newport DJ, Bonsall R, Miller AH, Nemeroff CB. Altered pituitary-adrenal axis responses to provocative challenge tests in adult survivors of childhood abuse. Am J Psychiatry. 2001; 158(4):575–581. [PubMed: 11282691]
40. Allsworth JE, Zierler S, Krieger N, Harlow BL. Ovarian function in late reproductive years in relation to lifetime experiences of abuse. Epidemiology. 2001; 12(6):676–681. [PubMed: 11679796]
41. Repetti R, Taylor SE, Seeman TE. Risky families: family social environments and the mental and physical health of offspring. Psychological Bulletin. 1999; 128(2):330–366. [PubMed: 11931522]
42. Gunnar M, Gonzalez DA, Goodlin BL, Levins S. Behavioral and pituitary-adrenal response during a prolonged separation period in rhesus monkeys. Psychoneuroendocrinology. 1981; 6:65–75. [PubMed: 7195597]
43. Brown J, Cohen P, Chen H, Smailes E, Johnson JG. Sexual Trajectories of Abused and Neglected Youths. J Dev Behav Pediatr. 2004; 25(2):77–82. [PubMed: 15083128]
44. Spatz Widom C, Kuhns JB. Childhood victimization and subsequent risk for promiscuity, prostitution, and teenage pregnancy: a prospective study. American Journal of Public Health. 1996; 86(11):1607–1612. [PubMed: 8916528]
45. Schwartz SM. Invited commentary: Studying the epidemiology of uterine leiomyomata--past, present, and future. Am J Epidemiol. 2001; 153(1):27–29. discussion 30. [PubMed: 11159142]
46. Luoto R, Rutanen E, Auvinen A. Fibroids and Hypertension: A Cross-Sectional Study of Women Undergoing Hysterectomy. Journal of Reproductive Medicine. 2001; 46:359–364. [PubMed: 11354837]
47. Manuck SBKA, Muldoon MF. Behaviorally-evoked cardiovascular reactivity and hypertension: conceptual issues and potential associations. Ann Behav Med. 1990; 12:3–16.
48. Riley EH, Wright RJ, Jun HJ, Hibert EN, Rich-Edwards JW. Hypertension in adult survivors of child abuse: observations from the Nurses' Health Study II. J Epidemiol Community Health. May; 64(5):413–418. [PubMed: 20445210]
49. Fonseca H, Ireland M, Resnick MD. Familial correlates of extreme weight control behaviors among adolescents. Int J Eat Disord. 2002; 32(4):441–448. [PubMed: 12386908]
50. Wonderlich SA, Wilsnack RW, Wilsnack SC, Harris TR. Childhood sexual abuse and bulimic behavior in a nationally representative sample. Am J Public Health. 1996; 86:1082–1086. [PubMed: 8712265]
51. Cramer SF, Horiszny JA, Leppert P. Epidemiology of uterine leiomyomas. With an etiologic hypothesis. J Reprod Med. 1995; 40(8):595–600. [PubMed: 7473458]
52. Faerstein E, Szklo M, Rosenshein NB. Risk factors for uterine leiomyoma: a practice-based case-control study. II. Atherogenic risk factors and potential sources of uterine irritation. Am J Epidemiol. 2001; 153(1):11–19. [PubMed: 11159140]
53. Baird DD, Travlos G, Wilson R, et al. Uterine Leiomyomata in Relation to Insulin-Like Growth Factor-I, Insulin, and Diabetes. Epidemiology. Mar 19.2009
54. Sadlonova J, Kostal M, Smahelova A, Hendl J, Starkova J, Nachtigal P. Selected metabolic parameters and the risk for uterine fibroids. Int J Gynaecol Obstet. Jul; 2008 102(1):50–54. [PubMed: 18336822]
55. Takeda T, Sakata M, Isobe A, et al. Relationship between metabolic syndrome and uterine leiomyomas: a case-control study. Gynecol Obstet Invest. 2008; 66(1):14–17. [PubMed: 18230910]
56. Bonomi AE, Anderson ML, Rivara FP, et al. Health care utilization and costs associated with childhood abuse. J Gen Intern Med. Mar; 2008 23(3):294–299. [PubMed: 18204885]
57. Paras ML, Murad MH, Chen LP, et al. Sexual abuse and lifetime diagnosis of somatic disorders: a systematic review and meta-analysis. JAMA. Aug 5; 2009 302(5):550–561. [PubMed: 19654389]
58. Weitlauf JC, Frayne SM, Finney JW, et al. Sexual violence, posttraumatic stress disorder, and the pelvic examination: how do beliefs about the safety, necessity, and utility of the examination influence patient experiences? J Womens Health (Larchmt). Jul; 2010 19(7):1271–1280. [PubMed: 20509787]

59. Margolin G, Gordis EB. The effects of family and community violence on children. Annu Rev Psychol. 2000; 51:445–479. [PubMed: 10751978]
60. Golier J, Yehuda R. Neuroendocrine activity and memory-related impairments in posttraumatic stress disorder. Development and Psychopathology. 1998; 10:857–869. [PubMed: 9886230]
61. Widom CS, Shepard RL. Accuracy of adult recollections of childhood victimization: part I. childhood physical abuse. Psychol Assess. 1996; 8(4):412–421.
62. Brewin CR, Andrews B, Gotlib IH. Psychopathology and early experience: a reappraisal of retrospective reports. Psychol Bull. Jan; 1993 113(1):82–98. [PubMed: 8426875]
63. Hardt J, Rutter M. Validity of adult retrospective reports of adverse childhood experiences: review of the evidence. J Child Psychol Psychiatry. 2004; 45(2):260–273. [PubMed: 14982240]
64. Briere J, Elliott DM. Prevalence and psychological sequelae of self-reported childhood physical and sexual abuse in a general population sample of men and women. Child Abuse Negl. 2003; 27(10):1205–1222. [PubMed: 14602100]
65. Herman-Giddens M, Sandler AD, Friedman NE. Sexual precocity in girls. An association with sexual abuse? Am J Dis Child. 1988; 142(4):431–433. [PubMed: 3348186]
66. Dong M, Anda RF, Dube SR, Giles WH, Felitti VJ. The relationship of exposure to childhood sexual abuse to other forms of abuse, neglect, and household dysfunction during childhood. Child Abuse Negl. 2003; 27(6):625–639. [PubMed: 12818611]
67. McLoyd V. Socioeconomic disadvantage and child development. Am Psychol. 1998; 53(2):185–204. [PubMed: 9491747]
68. Chen E, Matthews KA, Boyce WT. Socioeconomic differences in children's health: how and why do these relationships change with age? Psychological Bulletin. 2002; 128(2):295–329. [PubMed: 11931521]

Table 1

Frequency of abuse in childhood or adolescence: Nurse's Health Study II (reported in 2001) (n = 60,615)

	No. (%)
Cumulative Abuse History	
No exposure to violence	21,348 (35)
Mild/Moderate Single Type	22,687 (37)
Mild-Multiple or Severe-Single Type(s)	9182 (15)
Moderate-Chronic or -Multiple Types	4566 (8)
Severe-Chronic or -Multiple Types	1730 (3)
Severe Chronic and Multiple Types	1102 (2)
Childhood Trauma Questionnaire Score	
5 (None)	6972 (11.5)
6–10	32,642 (54)
11–15	13,742 (23)
16–20	5166 (8.5)
21–25	2093 (3)
Abuse Severity	
Severity of Physical Abuse	
None	28,561 (47)
Mild	11,389 (19)
Moderate	15,690 (26)
Severe	4975 (8)
Severity of Sexual Abuse	
None	40,761 (67)
Sexual Touching as Child or Teen	13,331 (22)
Forced Sexual Activity as Child or Teen	4981 (8)
Forced Sexual Activity as Child &Teen	1542 (3)
Abuse Type	
None	21,348 (35)
Physical abuse only	19,413 (32)
Sexual Abuse only	7213 (12)
Physical and sexual abuse	12,641 (21)

Table 2

Age-adjusted distribution of potential risk factors for ultrasound- or hysterectomy-confirmed uterine leiomyoma according to early life exposure to violence (childhood or adolescence) among premenopausal women: Nurse's Health Study II, 1989 (n = 60,615)

	Cumulative Exposure to Violence in Early Life					
Characteristic[a]	**No Abuse (n = 21,348)**	**Mild/Moderate Single (n = 22,687)**	**Mild-Multiple or Severe-Single) (n = 9182)**	**Moderate-Chronic or – Multiple (n = 4566)**	**Severe-Chronic or – Multiple (n = 1730)**	**Severe Chronic & Multiple (n = 1102)**
Age; mean (SD)	34 (5)	34 (5)	34 (5)	34 (5)	35 (5)	35 (4)
BMI (kg/m^2); mean (SD)	24 (5)	24 (5)	24 (5)	24 (5)	25 (5)	25 (6)
Hypertension (%)	4084 (19)	4501 (20)	2038 (22)	1024 (22)	460 (26)	327 (29)
Parent education < High School	569 (3)	736 (3)	399 (4.3)	204 (4.5)	79 (4.5)	46 (4.2)
Emotional neglect in childhood	1227 (6)	2634 (12)	1599 (17)	1171 (26)	1201 (30)	498 (45)
Ever married	18,306 (86)	19,728 (87)	8057 (88)	3981 (87)	1526 (88)	943 (85)
Age at menarche ≤11 years	4789 (22)	5291 (23)	2376 (26)	1184 (26)	515 (30)	329 (30)
Ever Pregnant	5317 (75)	4862 (79)	1772 (80)	868 (81)	316 (81)	225 (79)
Age at first birth ≤24 years	4854 (23)	5843 (26)	2694 (29)	1453 (32)	616 (35)	418 (38)
Time since last birth (months); mean (SD)	70 (58)	71 (59)	75 (61)	78 (62)	83 (65)	88 (66)
History of infertility	3579 (17)	3983 (18)	1603 (17)	837 (18)	353 (20)	233 (21)
Oral Contraceptive use						
Current	3114 (14)	2985 (13)	1188 (13)	559 (12)	202 (12)	121 (12)
Never	3962 (19)	3868 (17)	1327 (15)	636 (14)	223 (13)	137 (13)
First use age 13–16 years	775 (3.6)	1059 (4.7)	591 (6.5)	361 (7.9)	169 (10)	120 (11)
>40 Day menstrual cycle	1567 (7)	1567 (7)	676 (7)	324 (7)	137 (8)	98 (9)
Race						
White	20,090 (94)	21,190 (93)	8452 (92)	4227 (93)	1595 (92)	1013 (92)
Black	139 (0.7)	210 (0.9)	141 (1.5)	51 (1.1)	26 (1.5)	12 (1.1)
Latina	155 (0.7)	294 (1.3)	166 (1.8)	79 (1.7)	39 (2.3)	24 (2.2)
Asian	283 (1.3)	333 (1.5)	152 (1.7)	64 (1.4)	27 (1.6)	21 (1.9)
Race/ethnicity missing	681 (3.2)	660 (2.9)	271 (3.0)	145 (3.2)	43 (2.5)	32 (2.9)
Annual breast exam	19,535 (91)	20,722 (91)	8321 (91)	4144 (91)	1557 (90)	993 (90)

[a] No. (%), unless otherwise indicated

Table 3

Incidence rate ratios of ultrasound- or hysterectomy-confirmed uterine leiomyomata among premenopausal women according to severity, chronicity, and type of violence exposure in childhood or adolescence: Nurse's Health Study II (1989–2005)

Characteristics	No. Woman- Years	No. Cases	Model 1[a]	Model 2[b]	Model 3[c]
Cumulative Abuse History					
No exposure to violence [d]	262,132	3214	1.00	1.00	1.00
Mild/Moderate Single Type	272,888	3656	1.09 (1.04– 1.14)	1.08 (1.03– 1.14)	1.08 (1.03– 1.13)
Mild-Multiple or Severe-Single Type(s)	108,717	1648	1.21 (1.14– 1.28)	1.18 (1.11– 1.25)	1.17 (1.10– 1.24)
Moderate-Chronic or -Multiple Types	53,334	858	1.30 (1.21– 1.40)	1.24 (1.15– 1.34)	1.23 (1.14– 1.33)
Severe-Chronic or -Multiple Types	19,696	333	1.34 (1.20– 1.50)	1.25 (1.11– 1.40)	1.24 (1.10– 1.39)
Severe Chronic and Multiple Types	12,099	225	1.53 (1.33– 1.75)	1.39 (1.14– 1.57)	1.36 (1.18– 1.54)
Childhood Trauma Scale Score					
0–5[d]	83,900	1025	1.00	1.00	1.00
6–10	397,576	5126	1.09 (1.02– 1.16)	1.09 (1.02– 1.17)	1.09 (1.02– 1.16)
11–15	163,933	2382	1.21 (1.12– 1.30)	1.20 (1.11– 1.29)	1.18 (1.10– 1.28)
16–20	60,394	993	1.36 (1.25– 1.49)	1.33 (1.21– 1.45)	1.31 (1.20– 1.43)
21–25	23,061	412	1.46 (1.29– 1.63)	1.37 (1.22– 1.54)	1.35 (1.20– 1.51)
Abuse Severity[e]					
Severity of Physical Abuse					
None[d]	347,838	4407	1.00	1.00	1.00
Mild	137,116	1879	1.08 (1.02– 1.14)	1.08 (1.03– 1.15)	1.09 (1.03– 1.15)
Moderate	186,865	2711	1.11 (1.06– 1.16)	1.10 (1.05– 1.15)	1.10 (1.04– 1.15)
Severe	57,046	941	1.21 (1.12– 1.30)	1.16 (1.08– 1.25)	1.16 (1.07– 1.25)
Frequency of Sexual Abuse					
None[d]	495,550	6365	1.00	1.00	1.00
Sexual Touching as Child or Teen	157,884	2346	1.11 (1.06– 1.17)	1.10 (1.04– 1.15)	1.09 (1.04– 1.14)
Forced Sexual Activity as Child or Teen	58,057	918	1.19 (1.11– 1.27)	1.12 (1.05– 1.21)	1.12 (1.04– 1.21)
Forced Sexual Activity as Child &Teen	17,374	309	1.28 (1.14– 1.44)	1.18 (1.05– 1.33)	1.16 (1.03– 1.31)
Type of Abuse[e]					
None [d]	262,132	3214	1.00	1.00	1.00

Characteristics	No. Woman- Years	No. Cases	Model 1[a]	Model 2[b]	Model 3[c]
Physical abuse only	233,418	3151	1.10 (1.05– 1.15)	1.09 (1.04– 1.15)	1.09 (1.04– 1.15)
Sexual Abuse only	85,706	1193	1.12 (1.05– 1.19)	1.09 (1.02– 1.17)	1.09 (1.02– 1.16)
Physical and sexual abuse	147,609	2380	1.29 (1.22– 1.36)	1.24 (1.17– .30)	1.23 (1.16– 1.29)

[a] Model 1 controls for age, parental education, and race/ethnicity

[b] Model 2 controls for all variables in Model 1 and parity (1, 2, ≥3 pregnancies >6 months); age of menarche (≤10, 11, 12, 13, 14,15,16, ≥17 years of age); age of first oral contraceptive use (never, 13–16, 17–20, 21–24 years); age of first birth (≤22, 23–25, ≥25 years of age); time since last birth (1–7, 8–15, ≥16 years); history of infertility (yes, no); menstrual irregularity (regular, somewhat irregular or 21–30 day cycle, very irregular >40 day cycle).

[c] Model 3 controls for all variables in Model 2 and BMI (continuous); diastolic blood pressure (continuous).

[d] Reference category.

[e] Models mutually adjust for physical and sexual abuse;