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Cervical Neoplasia-Related Factors and Decreased Prevalence of Uterine Fibroids among a Cohort of African-American Women

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Abstract

Objective—To investigate whether the previously reported inverse association between cervical neoplasia and uterine fibroids is corroborated.

Design—Cross-sectional analysis of enrollment data from an ongoing prospective study of fibroid development.

Setting—Detroit, Michigan area.

Patients(s)—Self-reported data on abnormal Pap smear, colposcopy and cervical treatment were obtained from 1,008 African-American women ages 23-34 with no previous fibroid diagnosis and no reported history of HPV vaccination. Presence of fibroids was assessed at a standardized ultrasound examination.

Intervention(s)—None.

Main Outcome Measure(s)—The association between the 3 cervical neoplasia-related variables and presence of fibroids was evaluated with logistic regression to estimate age-adjusted and multivariable-adjusted odds ratios (ORs).

Result(s)—Of the analysis sample, 46%, 29% and 14% reported a prior abnormal Pap smear, colposcopy and cervical treatment, respectively. Twenty-five percent had fibroids at ultrasound. Those reporting cervical treatment had a 39% [aOR: 0.61, 95%CI (0.38-0.96)] reduction in fibroid risk. Weak non-significant associations were found for abnormal Pap smear and colposcopy.

Conclusion(s)—Although a protective-type association of cervical neoplasia with uterine fibroids seems counter intuitive, a causal pathway is possible, and the findings are consistent with

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Capsule: As in two previous studies, a measure of cervical neoplasia was associated with decreased risk of fibroids (those with history of cervical treatment had a 39% adjusted reduction in odds).

two prior studies. Further investigation is needed on the relationship between fibroids and cervical neoplasia and HPV-related mechanisms.

Keywords

Uterine Fibroids; Cervical Neoplasia; Cervical Treatment; Abnormal Pap Smear; Colposcopy

Introduction

Uterine fibroids are one of the most common gynecologic conditions affecting women during their reproductive years (1). Symptoms resulting from fibroids (pain, severe bleeding, reproductive problems) are the leading reason for hysterectomy in the United States (US), accounting for 40% of all hysterectomies, or approximately 240,000 hysterectomies per year (2). One US study found an estimated cumulative incidence of fibroid tumors by age 50 of >80% for African-American women and close to 70% for White women (3). Pathology data based on a systematic search of 100 sequential hysterectomy specimens that were thinly sliced for analysis show comparable prevalence estimates (4).

The etiologic cause of fibroids is largely unknown, although selected risk factors have been established such as African-American heritage, older age (up to the age of menopause), younger age at menarche, and nulliparity (5-7). Other factors such as BMI, smoking, hormonal contraceptive use and alcohol, have been inconsistently associated with fibroid risk (5, 8, 9). A hypothesis was postulated decades ago that reproductive tract infections may play a role in fibroid development (10); however, there are limited data that examine associations between reproductive tract infections and fibroid risk (5).

One clinic-based case-control study found a positive association and dose-response relationship between pelvic inflammatory disease (PID), the number of PID episodes and uterine fibroids among premenopausal women (11). No association was found between self-reported history of genital herpes or warts and fibroids, although a non-significant increased risk of fibroids was observed for women with self-reported history of *Chlamydia trachomatis* infection. The Uterine Fibroid Study found no association between PID and uterine fibroids for both African-American and White women, and positive non-significant associations for self-reported history of Chlamydia infection in White women, and trichomonas, syphilis, and “other infections” in African-American women; self-reported history of genital herpes was found to have a non-significant positive association in both ethnic groups (5). Interestingly, and counter intuitively, in both of these studies (5, 11), self-reported history of abnormal Pap smear was inversely associated with fibroids.

In the current study we explored the relationship between uterine fibroids and women's reported history of abnormal Pap smears. We also investigated additional markers of cervical pathology that are even more closely linked to more severe stages of cervical neoplasia, colposcopy (procedure performed after an abnormal Pap result to further examine the cervix and biopsy lesions) and treatment for cervical dysplasia (i.e. cone biopsy, loop excision, cryotherapy, or laser treatment conducted after colposcopy to remove or destroy abnormal cells).

Materials and Methods

Study Participants

We used enrollment data from an ongoing study, the Study of Environment, Lifestyle & Fibroids (SELF). SELF is a prospective cohort study of fibroid development. From November 2010 to December 2012, the study enrolled a volunteer sample of approximately

1,700 African-American women ages 23-34 without a diagnosis of fibroids. Enrollment data is currently available for the first 1,199 participants. Recruitment was designed to saturate the recruitment area (Detroit, Michigan and surrounding area) with information about the study. Materials included a website (detroitself.org), fliers, brochures at healthcare clinics, local radio, television, newspaper, and magazine advertisements, information booths at community events, and letters to women who had been seen in the past year by a doctor at Henry Ford Health System (HFHS), a large medical provider in the Detroit area and collaborating institution. The letters were sent to women listed as 23-34 years of age, with stratification by age to help maintain equal recruitment by age. This age group was chosen based on ultrasound screening data (12) to capture women early enough in order to have a sizeable proportion without fibroids.

Women who were interested in learning more about the study, phoned the study number, and could be screened for eligibility. Women were not eligible for SELF if they had previously been diagnosed with uterine fibroids, had a hysterectomy, had ever taken medication to treat lupus, Grave's disease, Sjogren's scleroderma or multiple sclerosis, or ever had any type of cancer treated with radiation or chemotherapy. Eligible women with further interest received detailed information about the study during an orientation session. Those who chose to enroll after the orientation gave informed consent and completed self-administered questionnaires, a telephone interview, and had a standardized research ultrasound examination to screen for the presence of fibroids. Some women had uterine fibroids at enrollment of which they were unaware.

Women pregnant at recruitment are delayed enrollment until 4 months after delivery so that pregnancy does not interfere with ultrasound assessment of fibroids. SELF participants will be followed for at least five years after enrollment with subsequent ultrasound examinations every 20 months. Women who screened negative at enrollment will be followed for fibroid development; women who screened positive at enrollment and those who develop incident fibroids will be followed for development of additional fibroids and fibroid growth. The study was approved by the institutional review boards of the National Institute of Environmental Health Sciences and Henry Ford Health.

Study participants were excluded if they reported being vaccinated with at least 1 HPV shot (3 given for full protection) (n=191, 16%). These women would be less likely to have a history of cervical neoplasia since it is highly linked to HPV infection. Thus, 1,008 participants were eligible for this analysis. The women ineligible differed from eligible participants in regards to age. Those reporting at least 1 HPV shot were younger than those reporting no shots, which is expected since the HPV vaccine has been recommended since 2006 for women 26 and younger.

Cervical Neoplasia-Related Variables

Three cervical neoplasia-related variables were evaluated in this study: self-reported previous abnormal Pap smear (yes/no), colposcopy (yes/no) and colposcopy follow-up with cervical treatment i.e. cone biopsy, loop electrosurgical excision procedure (LEEP), cryotherapy, or laser treatment (yes/no). Women were not asked to report the specific findings of the abnormal Pap smears or colposcopies, nor were they queried about history of endometrial curettage. Participants could only answer questions regarding cervical treatments if they answered yes to either having had a previous abnormal Pap smear or colposcopy.

Fibroid Assessment

The outcome for this study was fibroid presence (yes/no) at the transvaginal ultrasound examination completed at enrollment. Ultrasound is the standard procedure for the detection and diagnosis of fibroids (13). It is as accurate as magnetic resonance imaging for women with no more than four fibroids (13). If there were problems with transvaginal visualization, an abdominal scan was also completed. Focal fibroids of 0.5 cm diameter or greater were recorded. A data-collection form designed for the study was completed by the sonographer for each examination which included documentation of size of largest fibroid if any were present.

All ultrasounds were conducted by sonographers at one of 3 HFHS clinics. In order to ensure the quality of these ultrasound data, study sonographers were required to have at least 3 years of experience in gynecologic ultrasound, receive formal training for the study, and be individually monitored by the head sonographer during their first 10 study examinations. A video clip of the uterus and still images of all measurements were archived for each ultrasound examination and a random selection of 8% of each sonographer's ultrasound examinations, stratified to oversample participants with fibroids, were checked by comparing the data collected with the archived images.

Statistical Analysis

Distributions of covariates were compared among the cervical neoplasia-related variables. The association between the 3 variables and presence of fibroids was assessed with multivariable logistic regression. Models were fitted to estimate age-adjusted and multivariable-adjusted odds ratios (ORs) and associated 95% confidence intervals (CIs). In addition to the 3 cervical neoplasia-related variables, we evaluated age-adjusted ORs and 95% CIs for each type of cervical treatment and fibroids (with “no treatment” as the referent group).

Potential confounders for multivariable analyses were evaluated using the change in estimate approach. If the dropping of the variable changed the β-coefficient for the cervical neoplasia-related variable by 10% or more the variable was kept in the final model; otherwise it was dropped. Age (continuous), age of menarche (continuous) and parity (nulliparous vs. parous) were included a-*priori* based on their established associations with uterine fibroids (5-7).

The other covariates of interest based on the literature included: education (high school/general education development (GED) or less, some college/associates/technical, bachelors/masters/PhD), body mass index (BMI) (<25, 25-29, 30-34, ≥35) in kg/m^2, smoking status (never, former, current), number of sex partners before the age of 20 (1 or less, 2 to 5, 6+), self-reported prior diagnosis of Chlamydia (yes/no), self-reported prior diagnosis of genital herpes (yes/no), and alcohol drinking. The alcohol variable reflected the drinking level each woman reported for the age(s) when she was drinking the most. Non/light drinkers were those who never had 10 or more drinks in a year. Moderate drinkers were those who drank no more than 5 drinks on days when they drank and had four or more drinks per sitting no more than once per month. Heavy drinkers were those who usually drank 6 or more drinks on days when they drank or drank 4+ drinks per sitting at least 2 to 3 times a month. Data were rarely missing and complete case analysis was performed.

In addition, we looked at the ORs and 95% CIs for cervical treatment and size of fibroids (diameter of the largest fibroid) using multivariable-adjusted multinomial logistic regression with a 3-level outcome variable: no fibroids, small fibroids (<2cm), large fibroids (≥2cm). The no fibroid group was the referent group.

To evaluate the robustness of our findings, we examined multivariable-adjusted ORs and 95% CIs for the association of cervical treatment with fibroids in a series of sensitivity analyses by restricting or stratifying the sample. To minimize variability in access to care, we limited the sample first to participants who reported no difficulty accessing care (n=662) and second to participants who reported having a pelvic exam in the past 2 years (n=803). To reduce potential unmeasured confounding by smoking, an independent risk factor for cervical neoplasia, we limited participants to those who reported never smoking (n=748). Lastly, to further investigate temporality, we dichotomized time since cervical treatment at the median (7 years) and looked at the association between treatment and fibroids for those who reported their first cervical treatment ≤7 years (n=81) and >7 years (n=65) before enrollment.

All analyses were conducted with SAS 9.3.

Results

Of the 1,008 women included, 46% (n=466) reported a prior abnormal Pap smear, 29% (n=290) reported a prior colposcopy and 14% (n=146) reported cervical treatment (Table 1). In addition, the first procedures/treatments were reported to occur a median of 7 years prior to enrollment (Table 1). Those with a prior history of abnormal Pap smears, colposcopy or cervical treatment tended to: be older, more educated, have less difficulty seeing a doctor, be less likely to be current smokers, have more sex partners before age 20, be more likely to self-report being diagnosed with Chlamydia or genital herpes, and be parous than those without a prior history (Table 1). Twenty-five percent (25%) of women had fibroids discovered at ultrasound screening.

In multivariable analyses, only the *a-priori* variables (age, age of menarche and parity) remained in the model. No other covariates were found to be confounders of the association between the cervical neoplasia-related variables and the outcome. Age-adjusted and multivariable adjusted estimates were very similar (Table 2). In multivariable-adjusted analyses, those with a previous abnormal Pap smear had a non-significant 13% reduction in the odds of fibroids [aOR: 0.87 95%CI (0.64-1.18)], those with a colposcopy had a nonsignificant 12% reduction [aOR: 0.88 95%CI (0.63-1.23)] and those with cervical treatment had a 39% reduction [aOR: 0.61 95%CI (0.38-0.96)]. The inverse association with treatment appeared stronger for women whose largest fibroid was ≥2cm in diameter (n=104) compared to women with fibroids <2cm (n=145) [aOR: 0.45 95%CI (0.21-0.93) for women with large fibroids; aOR: 0.73 95%CI (0.42-1.25) for women with small fibroids].

Furthermore, the association of cervical treatment and fibroids remained consistent across the different sensitivity analyses (Figure 1). The age-adjusted OR for each of the cervical treatments is shown in Table 3. Each tended to be inversely related to fibroids though all sample sizes were small.

Discussion

We found an inverse association between cervical treatment, which is an indicator of severe cervical neoplasia, and uterine fibroids. Weak, non-significant inverse associations were seen between history of abnormal Pap smear or colposcopy and uterine fibroids. The inverse association between cervical treatment and fibroids tended to be stronger for women with larger fibroids than those with small fibroids.

Prior literature on cervical neoplasia-related variables and fibroids is limited. Two prior studies found a protective association between self-reported abnormal Pap smear and

fibroids. The first was a clinic-based case-control study among 318 premenopausal women in Baltimore, MD (11). The second was the Uterine Fibroid Study that screened randomly-selected 35-49 year-olds for fibroids with ultrasound (5).

Twenty-five percent (25%) of our cohort of African-American women of childbearing age had fibroids at ultrasound screening. This prevalence falls within the range of prior US studies that conducted ultrasound screening for fibroids in African-Americans (3, 5, 12). Nearly half our sample reported a history of abnormal Pap smears. This is plausible given that most of our participants would have begun Pap smear screening under the old criteria which began at young ages for girls with early sexual intercourse (14) and resulted in high rates of detected naturally resolvable abnormalities (15). In our sample, 43% of those reporting abnormal smears had their first abnormal Pap smear before age 21.

This analysis had several strengths. We had extensive data to assess potential confounding, and we conducted sensitivity analyses to evaluate potential bias. We used enrollment data from an ongoing prospective study with a standardized measure of fibroid status based on systematic ultrasound screening. The size of the largest fibroid was systematically measured, so we could examine the association with small as well as large fibroids. We found that there tended to be a stronger inverse association between cervical neoplasia and large fibroids compared to small fibroids. Larger fibroids could be indicative of early onset or fast growth. Thus, future epidemiologic studies could further examine whether cervical neoplasia is related to inhibition of fibroid growth.

This analysis also had several limitations. We lacked information on the pathology results regarding the abnormal Pap smears/ colposcopies and whether biopsy or endocervical curettage was performed at the time of colposcopy. Cervical neoplasia-related variables were self-reported, which could be subject to recall error. The only paper of which we are aware that compared self-report of abnormal Pap smear to medical records found relatively good reporting, but they studied women in the UK (16). Given the invasiveness of the colposcopy and cervical treatment, these variables are likely to be reported even more accurately than abnormal Pap. We also had potential for selection bias. Participants who have a history of cervical abnormalities may be a more “highly screened” group and, thus, may also be more likely to have been diagnosed with fibroids which was a criterion for study exclusion. However, sub-setting the population to those with no difficulty accessing care as well as those who had a pelvic exam within the last 2 years did not impact the results.

The inverse association we and others have seen seems counterintuitive, but we could not explain it as bias. Uncontrolled confounding would likely bias results toward a positive, not inverse, association, and when we performed sensitivity analyses, we found no evidence that selection bias could account for the findings. A biological basis for the observed association may be plausible. Though this was a cross-sectional analysis, the temporality of events is consistent with involvement of a biological process, i.e., most participants would likely have had the cervical treatment prior to fibroid onset (median time between cervical treatment and fibroid screening was 7 years, the majority having their first abnormal Pap smear before age 21). In contrast, fibroid onset for African-Americans appears rare in the early 20's but begins to increase in the late 20's, possibly peaking in the 30's [reviewed in (5)]. We also found that the association between treatment and fibroids was essentially the same for those who reported their first cervical treatment ≤7 years vs. >7 years before enrollment (aORs = 0.59 and 0.62 respectively).

Biological mechanisms could involve human papillomavirus, given that cervical treatment is given in response to moderate or severe neoplasia which is associated with persistent HPV

infection (17). High-risk HPV prevalence is detected in up to 60% of abnormal Pap smear cases (18, 19), close to 70% of low-grade squamous intraepithelial lesion (LSIL) cases (20) and approximately 90% of high-grade squamous intraepithelial lesion (HSIL) cases (21). Persistent HPV infection in the cervical tissue is highly associated with integration of the HPV genome into the host genome (17, 22).

Much less is known about HPV infection of the endometrium and myometrium. However, finding HPV DNA in the upper tract is not uncommon. For example, it was reported in 10% of endometrial samples tested, with no differences seen between normal and cancerous tissue (23, 24). It has also been reported in placentae (24). Though it is thought that HPV selectively infects only basal cells of stratified epithelium, the infectious process is not understood (25), and to our knowledge myometrial and fibroid tissue have not been tested for HPV. One of the pathogenic pathways hypothesized for fibroid development involves myometrial hyperplasia that appears to originate adjacent to the stroma (26), so paracrine effects from the endometrium may play a role.

It is also interesting that one of the sites of HPV integration into the DNA is in the region of HMGA-2 a gene that has long been of interest in fibroid research (27). HPV integration can also affect gene expression remote from insertion sites by affecting methylation patterns (28). Alterations in methylation have been found to disrupt tumor-suppressor gene function in the cervix (29) where more severe disease (CIN2/3 and cancer) has been linked to higher methylation levels (30, 31). Thus, it is of interest that methylation changes have been implicated in the pathogenesis of fibroids (32-34). Another possible mechanism is HPV-induced enhancement of immune surveillance. The immune response generated as a result of HPV infection could possibly cause the immune system to identify and eliminate initial fibroid lesions.

In summary, the results of this epidemiologic study are consistent with the available literature and it is the first to specifically explore the relationship between colposcopy and cervical treatment and uterine fibroids. Future epidemiologic studies of cervical treatment and fibroids are needed using medical record data to better characterize the cervical abnormalities. Despite the counter-intuitive findings of a potentially protective effect of cervical neoplasia, there are speculative yet intriguing possibilities for biologically plausible effects on fibroid development mediated by persistent HPV infection. Laboratory studies of endometrial and myometrial tissue are needed to study possible HPV infection of these tissues.

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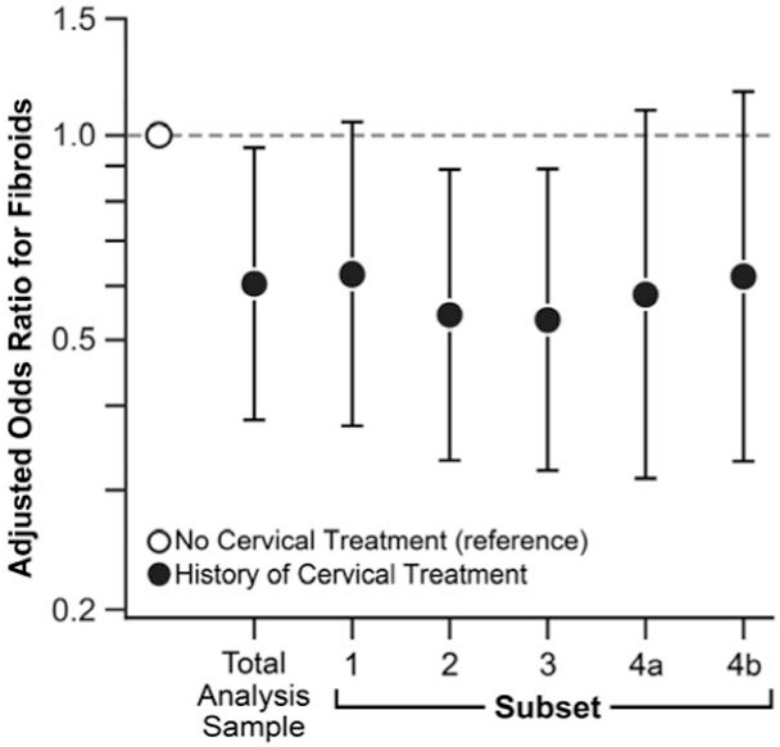

Figure 1.

Sensitivity analyses for the association of cervical treatment and uterine fibroids. The figure shows adjusted (for age, age of menarche and parity) odds ratios and 95% CIs. The sample sets are: entire analysis sample (n = 1,008), 1 = participants who reported no difficulty accessing care (n = 662), 2 = participants who reported having a pelvic exam in the past 2 years (n = 803), 3 = participants who reported never smoking (n = 748), 4a = participants who reported their first cervical treatment ≤7 years before enrollment (n=81) and 4b = participants who reported their first cervical treatment >7 years before enrollment (n=65).

Table 1

Characteristics of SELF Study Subjects[a] by Self-Reported Cervical Neoplasia-Related Variables (History of Abnormal Pap Smear, Colposcopy and Cervical Treatment)

	No History of Abnormal Pap Smear n=542 n (%)	History of Abnormal Pap Smear n=466 n (%)	History of Colposcopy[b] n=290 n (%)	History of Cervical Treatment[c] n=146 n (%)
Age at First Procedure/Treatment, median, IQR	----------	21 (19-24)	22 (19-25)	22.5 (19-25)
Time Since First Procedure/ Treatment, median, IQR	----------	8 (4-11)	7 (3-10)	7 (4-10)
Age (years), median, IQR	29 (26-32)	30 (27-32)	30 (27-32)	30.5 (28-33)
23-26 yrs	150 (28)	100 (21)	59 (20)	28 (19)
27-30 yrs	195 (36)	157 (34)	105 (36)	45 (31)
≥31 yrs	197 (36)	209 (45)	126 (43)	73 (50)
Education				
≤ High school/GED	141 (26)	79 (17)	45 (16)	19 (13)
Some college/ Associate/ Technical	264 (49)	225 (48)	134 (46)	74 (51)
Bachelors/Masters/Professional/ PhD	137 (25)	162 (35)	111 (38)	53 (36)
BMI (kg/m^2)				
16-24	108 (20)	81 (17)	55 (19)	28 (19)
25-29	102 (19)	99 (21)	64 (22)	37 (25)
30-34	112 (21)	97 (21)	64 (22)	28 (19)
≥ 35	220 (41)	189 (41)	107 (37)	53 (36)
Difficulty Seeing Doctor for Physical				
Not at all difficult	332 (61)	330 (71)	210 (72)	105 (72)
At least a little difficult	209 (39)	136 (29)	80 (28)	41 (28)
Missing	1	0	0	0
Last Pelvic Exam				
This year	185 (34)	189 (41)	119 (41)	62 (42)
Last year	214 (39)	215 (46)	131 (45)	67 (46)
At least 2 years ago	143 (26)	62 (13)	40 (14)	17 (12)
Smoking Status				
Never smoked	384 (71)	364 (78)	233 (80)	118 (81)
Former smoker	31 (6)	47 (10)	27 (9)	15 (10)
Current smoker	127 (23)	55 (12)	30 (10)	13 (9)
Drinking during heaviest period				
Non/Light	152 (28)	119 (26)	77 (27)	41 (28)
Moderate	183 (34)	167 (36)	103 (36)	54 (37)
Heavy	207 (38)	180 (39)	110 (38)	51 (35)
Age Started Menses (years), median, IQR	12 (11-13)	12 (11-13)	12 (11-13)	12 (10-12)
≤10 years	95 (18)	101 (22)	67 (23)	37 (25)

	No History of Abnormal Pap Smear n=542 n (%)	History of Abnormal Pap Smear n=466 n (%)	History of Colposcopy[b] n=290 n (%)	History of Cervical Treatment[c] n=146 n (%)
11 years	98 (18)	93 (20)	59 (20)	24 (16)
12 years	147 (27)	128 (27)	78 (27)	49 (34)
13 years	81 (15)	72 (15)	42 (14)	17 (12)
≥14 years	121 (22)	72 (15)	44 (15)	19 (13)
Number sex partners before 20				
≤1	161 (30)	93 (20)	62 (21)	30 (21)
2-5 people	255 (47)	240 (52)	150 (52)	78 (53)
≥ 6 people	125 (23)	132 (28)	77 (27)	38 (26)
Missing	1	1	1	0
Previous Chlamydia Diagnosis				
No	383 (71)	251 (54)	160 (55)	76 (52)
Yes	158 (29)	215 (46)	130 (45)	70 (48)
Missing	1	0	0	0
Previous Genital Herpes Diagnosis				
No	499 (92)	417 (89)	252 (87)	124 (85)
Yes	43 (8)	49 (11)	38 (13)	22 (15)
Parity				
Nulliparous	239 (44)	147 (32)	90 (31)	40 (27)
Parous	303 (56)	319 (68)	200 (69)	106 (73)

BMI, body mass index; GED, general education development;; IQR, interquartile range; SELF, Study of Environment, Lifestyle and Fibroids

Column percentages may not add to 100 due to rounding

[a] All subjects who have not had an HPV shot

[b] Two missing data on colposcopy

[c] Among subjects reporting history of abnormal Pap smear(s) and/or colposcopy

Table 2

Self-Reported Cervical Neoplasia-Related Variables Stratified by Fibroid Outcome Status

HPV-Related Variable	Fibroid Status		Odds Ratios	
	Yes n=249 n (%)	No n=759 n (%)	Age-Adjusted OR 95% CI	aOR[c] 95% CI
Abnormal Pap Smear				
Yes	110 (44)	356 (47)	0.83 (0.62-1.11)	0.87 (0.64-1.18)
No	139 (56)	403 (53)	1 (ref)	1 (ref)
Colposcopy[a]				
Yes	68 (27)	222 (29)	0.85 (0.62-1.18)	0.88 (0.63-1.23)
No	181 (73)	535 (71)	1 (ref)	1 (ref)
Cervical Treatment[b]				
Yes	27 (11)	119 (16)	0.59 (0.38-0.92)	0.61 (0.38-0.96)
No	222 (89)	640 (84)	1 (ref)	1 (ref)

CI, confidence interval; OR, odds ratio

Column percentages may not add to 100 due to rounding

[a] Two missing data on colposcopy

[b] Among subjects reporting history of abnormal Pap smear(s) and/or colposcopy

[c] Adjusted for age, age of menarche and parity

Table 3
Self-Reported Type of Cervical Treatment Stratified by Fibroid Status

Type of Cervical Treatment	Fibroid Status		
	Yes n (%) n=31	No n (%) n=151	Age-Adjusted OR[b] 95% CI
Laser	2 (6)	15 (10)	0.40 (0.09-1.77)
Cryotherapy	12 (39)	37 (25)	0.76 (0.39-1.50)
Cone Biopsy	6 (19)	51 (34)	0.32 (0.13-0.75)
LEEP	11 (35)	48 (32)	0.60 (0.30-1.18)
No Treatment	222	640	1 (ref)

CI, confidence interval; LEEP, loop electrosurgical excision procedure; OR, odds ratio

Column percentages may not add to 100 due to rounding

31 people reported more than 1 treatment