

Examining the Relationship Between Uterine Fibroids and Dyspareunia Among Premenopausal Women in the United States

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ABSTRACT

Introduction. Despite estimates of a high prevalence of deep dyspareunia (DD) among women in the United States, risk factors for this important area of sexual dysfunction have been largely understudied.

Aims. The purpose of this study was to examine the relationship between uterine fibroids and the prevalence of DD.

Methods. We used data from the Uterine Fibroid Study (enrollment 1996–1999 in a U.S. metropolitan area). Participating women were ages 35–49 and were randomly selected from the membership rolls of a prepaid health plan. Women were asked to provide detailed health information including a symptom questionnaire with questions about DD and to have a study ultrasound to screen for fibroids ≥ 0.5 cm in diameter. The analysis included 827 women, after restriction to participants who were premenopausal with an intact uterus, sexually active, completed the symptom questionnaire, and had fibroid status adequately assessed. Logistic regression was conducted to estimate the adjusted prevalence odds ratio (aPOR) for the association of DD with presence of fibroids after adjusting for age, ethnicity, education, depression, physical activity, parity, and pelvic pathology.

Main Outcome Measure. Our main outcome measures were the presence and severity of DD.

Results. The presence of fibroids was significantly associated with DD (aPOR = 1.7 95% confidence interval [CI] 1.1, 2.5). The aPOR was stronger for severe DD, DD that interfered with normal activity “some” or “a lot” (aPOR = 3.1 95% CI 1.2, 8.2). However, there was not a significant dose response relationship between fibroid burden (measured by uterine volume) and DD. Fundal fibroids were more strongly associated with DD than other fibroids. Additional factors associated with significantly elevated odds of DD were parity, depression, younger age, and pelvic pathology.

Conclusion. Our results suggest that fibroids are associated with DD. The association may not be causal but may reflect shared etiology and/or pathologic pathways. **Moshesh M, Olshan AF, Saldana T, and Baird D. Examining the relationship between uterine fibroids and dyspareunia among premenopausal women in the US. J Sex Med 2014;11:800–808.**

Key Words. Dyspareunia; Fibroids; Sexual Dysfunction; Pelvic Pain; Sexual Pain; Pelvic Pathology

Introduction

The causes and impact of deep dyspareunia (DD), a form of sexual dysfunction, have been largely understudied despite high prevalence estimates [1–3]. The importance of this lifestyle issue has gained recent attention because of studies that have revealed high prevalence of

sexual dysfunction among older menopausal women, but few data exist for premenopausal women [4]. Moreover, national attention and investigation of issues impacting relationship and marital quality have come to the forefront as the dissolution of marriage has remained high [5]. Although DD is only one small aspect of sexual dysfunction, it is thought to precede and worsen

other common sexual dysfunctions such as loss of desire, the most common sexual dysfunction seen in postmenopausal women [6].

Pelvic pathologic conditions such as endometriosis and interstitial cystitis are well-known and accepted contributors to the development of chronic pelvic pain, including dyspareunia; however, the importance of fibroids has not been as clear [6]. Previously reported associations between fibroids and DD have been weak to moderate in magnitude [7–9], requiring larger samples to more precisely estimate an association. Most studies were small, and only one used ultrasound to systematically detect fibroids [9]. The Uterine Fibroid Study (UFS) offered the opportunity to look at the association between fibroids and DD using a large population-based resource of primarily premenopausal African American and Caucasian women. We hypothesized that fibroids are a significant contributor to the presence and severity of DD among women.

Aims

- To examine the association between fibroids and DD
- To evaluate if fibroids contribute to dyspareunia severity (measured by DD interference with normal activity)
- To examine the dose response relationship between fibroid burden (measured by size of uterus) and DD
- To describe the contribution of other a priori chosen covariates toward the presence of DD

Methods

We used previously collected cross-sectional data from the UFS to conduct this analysis. The UFS enrolled a sample of 35 to 49-year-old women who were randomly selected from the membership rolls of a prepaid health plan located in Washington, DC. The response rate was over 80% with a total of 1,430 women participating in the initial enrollment during 1996–1999. The study has been described in detail [10]. Briefly, all women were asked to complete a self-administered questionnaire about medical history, dietary and occupational exposures, as well as symptoms related to fibroids. Premenopausal women were then screened with pelvic ultrasound to detect the presence of fibroids, regardless of prior clinical diagnosis. Women excluded from this analysis were

(i) women who were naturally or surgically menopausal including either a hysterectomy and/or a bilateral oophorectomy (n = 190); (ii) women who were not sexually active over the past year (n = 196); (iii) women who did not follow up to complete the symptom questions which included assessment of dyspareunia (n = 163); and (iv) women who did not have fibroid status determined (n = 55). This left a total of 827 women for this analysis (Figure 1). The UFS was approved by the National Institute of Environmental Health Sciences and George Washington University Human Subject Review Boards. Participants gave informed consent. This secondary data analysis was approved by the University of North Carolina at Chapel Hill IRB board.

Dyspareunia Assessment

Participants were asked to complete a self-administered questionnaire at enrollment, prior to ultrasound examination. DD was assessed with the following questions:

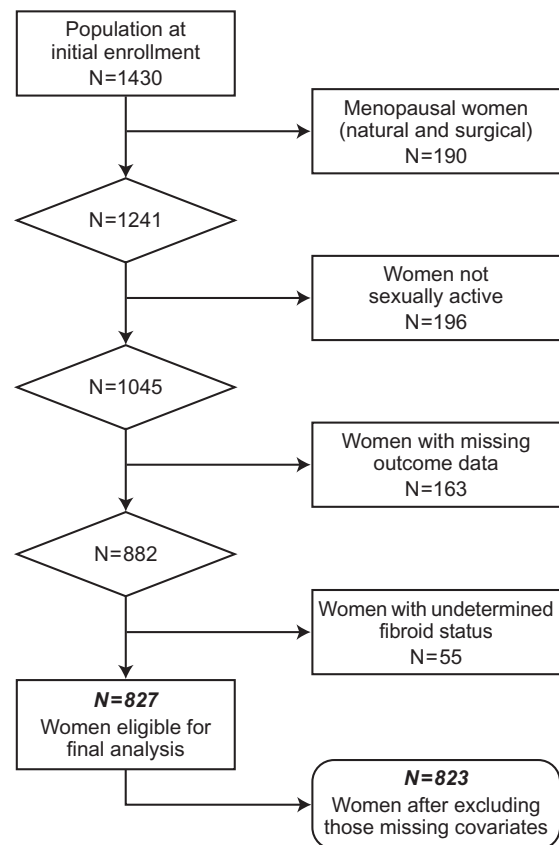


Figure 1 Participants in the NIEHS Uterine Fibroid Study selected for analysis of deep dyspareunia.

Have you experienced pain deep inside during sexual intercourse more than once or twice in the past 12 months?

- 1 Yes
- 2 No
- 3 Not having sex

If yes, on average, how many days do you experience this symptom?

- 1 Less than 1 day per month
- 2 1–4 days per month
- 3 More than 4 days a month

If yes, on days when you have this symptom, how much does it prevent you from carrying out your normal activities?

- 1 None or a little
- 2 Some
- 3 A lot

Women who answered yes were considered to have DD. Women who had DD that prevented normal activity “some” or “a lot” as contrast to “none” or “a little” were classified as having severe DD. Similar questions were asked regarding pain around the vaginal opening during sexual intercourse. Pain at the vaginal opening was not included as part of the main outcome measure but was included in the descriptive analysis. Thus, we had two outcome variables: (i) one variable that measured the presence or absence of DD (yes/no) and (ii) one variable that measured DD severity (i.e., DD_{severe} = pain that prevents normal activity “some” or a “lot”).

Main Outcome Measures

- DD: (yes/no)
- Severe DD: (DD_{severe} = pain that prevents normal activity “some” or a “lot”).

Fibroid Assessment

For participants who had undergone a recent clinic ultrasound examination at the participating clinic, we assigned fibroid status on the basis of that examination. Other participants were asked to undergo both a transvaginal and transabdominal study ultrasound to determine fibroid status. During the study ultrasound examination, the two largest fibroids over 2.0 cm in diameter were evaluated for size, location, and position. The evaluated fibroids were measured in three planes (longitudinal, anterior–posterior, and transverse). The number of fibroids was not systematically tracked, so women with numerous fibroids did

not have all fibroids evaluated. All sonographers were certified by the American Registry of Diagnostic Medicine and were under the supervision of a radiologist with fellowship training in sonography. A total of 78% ($n = 631$) had fibroid status determined by study ultrasound, and 22% ($n = 175$) had fibroid status determined by recent ultrasound exam. A total of 2.5% ($n = 21$) of women had fibroid status determined by self-report. We only used self-report data for women who reported “yes” when asked if they had a clinical diagnosis of fibroids because fibroids were frequently found at ultrasound that had not been previously diagnosed [10].

We classified fibroid burden in two ways. First, we created a dichotomous yes/no variable. Second, we created a four-level variable for fibroid burden as measured by uterine volume (no fibroids, fibroid/s present with uterine volume $<150 \text{ cm}^3$, fibroid/s present with uterine volume $\geq 150 \text{ cm}^3$ but $<300 \text{ cm}^3$, fibroid/s present with uterine volume $\geq 300 \text{ cm}^3$). Uterine volume was used as a measure of fibroid burden because only the two largest fibroids $\geq 2.0 \text{ cm}$ were measured. Therefore, we could not sum volumes across all fibroids.

Evaluated fibroids were also classified based on their location with respect to the uterine axis and the uterine layers. Fibroid location with respect to the uterine axis was defined as (i) fundus, upper third of the uterus; (ii) corpus, the middle third of the uterus; or (iii) lower uterine segment/cervix, lower third of the uterus. Location was recorded for the two largest fibroids $\geq 2.0 \text{ cm}$ in diameter. Evaluated fibroids were also classified with respect to the uterine layers. They could be (i) intramural, within the uterine wall; (ii) subserosal protruding outside the uterine wall; or (iii) submucosal, impinging on the uterine cavity.

Covariate Assessment

Potential confounders were chosen a priori on the basis of the literature. Some variables were assessed from the self-administered questionnaire (ethnicity, education, and history of depression; i.e., ever told by a doctor or a health care professional that she had depression). Other variables were assessed through a structured interview (age, number of deliveries, and physical activity). Alcohol and body mass index (BMI) were also evaluated as possible confounders but were not included in the final model as they did not influence the association observed between fibroids and DD. Self-reported ethnicity was categorized using disjoint indicator coding (African American,

Caucasian, and other). We did not distinguish between the type of delivery (C section or vaginal); however, approximately 20% (n = 163) of the study population had at least one C section, and 7% (n = 58) had two or more C sections.

The pelvic pathology variable included women with a self-reported history of at least one of the following: endometriosis, uterine prolapse, or interstitial cystitis (which was inferred by symptom history). Of the 77 women who reported the presence of pelvic pathology, 58 reported endometriosis as at least one of their diagnoses, 14 women reported having prolapse, and eight women reported frequent painful urination more than 4 days per month over the past year (some women reported more than one of these). Nonoccupational physical activity was categorized as vigorous, moderate, or mild (walking), and the number of hours per week doing these activities were recorded. A summary variable based on estimated metabolic scores for the activities was created (low = lowest 33% of the distribution, medium = middle 33%, high = 67th–83rd percentile, and very high = above the 83rd percentile) [11]. BMI was calculated based on measured weight from the study clinic visit and categorized as <25, 25–29, 30–34, and 35 and over. Alcohol use was assessed by interview and categorized by the number of drinks per week (0–0.5, 1–2, 3–6, and 7 or more).

Statistical Analysis

Chi-squared statistics were used to assess descriptive differences in proportions of associated symptoms between women with DD and women without DD. Multivariate logistic regression analysis was used to assess the relationship between the presence of fibroids and DD. Multinomial logistic regression was used to assess the relationship between the presence of fibroids and severe DD (DD that prevented normal activity “some” or “a lot”). Covariates were modeled using the categorizations shown in Table 1, except age and number of deliveries which were both kept as continuous variables.

Prevalence odds ratios (PORs) and 95% confidence intervals (CIs) were calculated. PORs were adjusted for age, ethnicity, education, number of previous deliveries, depression history, preexisting diagnosis of pelvic pathology, and physical activity. To evaluate the association between the presence of fibroids and severe DD, we created a three-tier outcome variable for DD (No DD, DD_{mild} = pain that prevents normal activity “none” or “a little”, and DD_{severe} = pain that prevents normal activity

Table 1 Characteristics of the study sample, National Institute of Environmental Health Sciences (NIEHS) Uterine Fibroid Study, stratified by deep dyspareunia status

Population Characteristics	No N = 668 n (%) [†]	Yes N = 159 n (%) [†]
Fibroids present		
Yes	410 (61)	113 (71)
No	258 (39)	46 (29)
Fibroid burden (size of largest fibroid) [‡]		
0.5 cm–3.9 cm	289 (70)	80 (71)
4.0 cm & over	121 (30)	33 (29)
Fibroid burden (uterine volume with fibroids present) [‡]		
Uterine Volume + fibroid <150 cm ³	225 (55)	64 (57)
Uterine Volume + fibroid 150 cm ³ –299 cm ³	133 (32)	35 (31)
Uterine Volume + fibroid 300 cm ³ & Over	52 (13)	14 (12)
Age		
35–39	222 (33)	72 (45)
40–44	247 (37)	58 (36)
45–50	199 (30)	29 (18)
Ethnicity		
White	259 (39)	36 (23)
Black	353 (53)	114 (72)
Other	56 (8)	9 (6)
Education		
High school/or less	88 (13)	31 (20)
Some college	194 (29)	65 (41)
College	171 (26)	38 (24)
Post graduate education	215 (32)	25 (16)
Number of deliveries		
0	223 (33)	33 (21)
1	133 (20)	35 (22)
2	213 (32)	47 (30)
3 or more	99 (15)	44 (28)
Missing	0	1
Depression		
No	566 (85)	116 (73)
Yes	102 (15)	42 (27)
Pelvic pathology [§]		
No	618 (93)	132 (83)
Yes	50 (7)	27 (17)
Physical activity [#]		
Low	226 (34)	54 (34)
Medium	225 (34)	49 (31)
High	110 (16)	29 (18)
Very high	106 (16)	25 (16)
Missing	1	2
Alcoholic drinks per week		
0–0.5	234 (35)	75 (47)
1–2	186 (28)	33 (21)
3–6	128 (19)	29 (18)
7 & over	120 (18)	22 (14)
Body mass index		
Under 25	280 (42)	55 (35)
25–29	192 (29)	41 (26)
30–34	89 (13)	34 (22)
35 & over	107 (16)	28 (18)
Missing	0	1
Abdominal cramps		
None	213 (32)	18 (11)
Less than 1 day per month	127 (19)	26 (16)
1–4 day per month	288 (43)	88 (55)
5 or more days per month	38 (6)	27 (17)
Missing	2	0
Abdominal bloating		
None	216 (32)	23 (14)
Less than 1 day per month	69 (10)	15 (9)
1–4 days per month	312 (47)	87 (55)
5 or more days per month	70 (11)	34 (21)
Missing	1	0
Pain at vaginal opening with intercourse		
No	632 (95)	104 (65)
Yes	35 (5)	55 (35)
Missing	1	0
Dyspareunia at age 30		
Never or less than one time per month	631 (95)	83 (52)
Once a month or more	24 (4)	73 (46)
Not sexually active at age 30	12 (2)	3 (2)
Missing	1	0

[†]Percentages are rounded.

[‡]Percentages calculated among only women with fibroids.

[§]Pelvic pathology included women who have a history of endometriosis, prolapse, or interstitial cystitis by symptom assessment.

[#]Physical activity is categorized as follows (low = 33rd percentile, medium = 33–66th, high = 67th–83rd percentile, very high = above the 83rd percentile.) Breakdown for physical activity obtained from Baird et al. [11]

Table 2 Fibroid status by DD frequency among women with DD ($N_{\text{total}} = 159$)

Pain frequency	All women N_{rowtotal}	Fibroids—no N (%) [†]	Fibroids—yes N (%) [†]
Less than 1 day per month	67	28 (42)	39 (58)
1–4 days per month	65	12 (18)	53 (82)
4 or more days per month	27	6 (22)	21 (78)

[†]Percentage calculations based on row total
DD = deep dyspareunia

“some” or “a lot”). To evaluate the dose response relationship between fibroid burden and DD, we calculated the POR for DD for each level of fibroid burden (as measured by uterine volume categories) and compared them with women with no fibroids as the reference group.

Exploratory analyses were conducted to see if our data are consistent with a prior report linking fundal fibroids to DD [9]. We evaluated if having a fibroid in the fundal location was a predictor of DD among women with fibroid location data ($n = 513$). Similar analysis was done to evaluate retroversion of the uterus as a predictor of DD. Our fundal location data are limited because we only evaluated a woman’s largest two fibroids ≥ 2.0 cm. Thus, our fibroid location analysis must be viewed as exploratory.

A supplemental analysis was conducted to investigate how the association between fibroids and DD may be modified by pelvic pathology. We stratified the analysis by the presence or absence of pelvic pathology. We conducted a likelihood ratio test (LRT) comparing the model with only the main effect of fibroids with the one with the added interaction term for pelvic pathology and fibroids. The alpha level of 0.10 for this test was chosen a priori.

All analysis was performed using SAS version 9.3 (SAS Institute, Cary, NC, USA), and Microsoft EXCEL version 2010 (Microsoft, Redmond, WA, USA) was used to conduct an LRT.

Results

Among women with fibroids, 22% ($n = 113$) reported the presence of DD over the past year, whereas only 15% ($n = 46$) of women with no fibroids reported DD (unadjusted P value_{difference} = 0.02). Compared with those without dyspareunia, women with the condition tended to be younger, African American, to have less education, more deliveries, to have reported a history of depression, and were more likely to have been diagnosed in the past with other pelvic pathology (endometriosis,

prolapse, and interstitial cystitis) (Table 1). Forty-six percent of those with DD reported that they also had this condition at age 30 compared with 4% of those without a current report of DD. Women with DD also had more pelvic and abdominal pain symptoms compared with those without DD (Table 1). Women with more frequent DD had a higher prevalence of fibroids than women with less frequent DD (Table 2). For example, 78% of the women who reported DD 4 or more days per month had fibroids, whereas 58% of those with DD less than 1 day a month had fibroids.

In the study sample, the POR between fibroids and DD (yes/no) after adjustment for age and ethnicity was 1.4 (95% CI 0.98, 2.18). Adjusting for age, ethnicity, number of deliveries, depression, physical activity, and education, the association between fibroids and DD was slightly stronger adjusted POR (aPOR) = 1.7 (95% CI 1.09, 2.54) (Table 3). Of the 159 participants reporting yes to DD, 34 women reported severe DD (pain that prevents normal activity “some” or “a lot”). In multinomial regression analysis adjusting for the same variables used in the overall DD analysis

Table 3 The association between fibroids and covariates with deep dyspareunia ($N_{\text{total}} = 823$)

Covariate	aPOR (95% CI)
Fibroids	1.7 (1.09, 2.54)
Age	0.9 (0.87, 0.96)
Education	0.8 (0.67, 1.03)
Ethnicity	
African American	1.00 (reference)
Caucasian	0.7 (0.44, 1.25)
Other	0.6 (0.26, 1.22)
Number of deliveries	1.3 (1.12, 1.54)
Depression	2.2 (1.45, 3.47)
Pelvic pathology [†]	2.8 (1.64, 4.77)
Physical activity [‡]	1.1 (0.90, 1.27)

[†]Pelvic pathology include women who have one of the following: endometriosis, prolapse, and/or interstitial cystitis

[‡]Physical activity is categorized (low = lowest 33% percent of combined activity, medium = 33–66% range of physical activity, high = 67th–83rd percentile of physical activity, very high = above the 83rd percentile in physical activity). Breakdown for physical activity variable came from Baird et al. [11]
aPOR = adjusted prevalence odds ratios; CI = confidence interval

Table 4 The association between fibroid burden and deep dyspareunia by uterine volume and by fibroid size

Covariate	Number of women N (%)	aPOR (95% CI)
Fibroid status		
No fibroids (reference)	304 (37)	1.00
Uterine volume <150 cm ³	289 (35)	1.8 (1.13, 2.80)
Uterine volume 150–299 cm ³	168 (20)	1.4 (0.84, 2.48)
Uterine volume 300 cm ³ and over	66 (8)	1.8 (0.83, 3.73)
Fibroid size		
No fibroids (reference)	304 (37)	1.00
Fibroid size 0.5–3.99 cm	369 (45)	1.64 (1.1, 2.55)
Fibroid size 4.0 cm and greater	154 (19)	1.74 (1.0, 3.05)

Adjusted for age, education, ethnicity, number of deliveries, depression, pelvic pathology, and physical activity
aPOR = adjusted prevalence odds ratios; CI = confidence interval

(yes/no), the association between fibroids and severe DD was stronger, aPOR_{DDsevere} = 3.1 (95% CI 1.20, 8.18).

When we examined the dose response relationship between fibroid burden (as measured by uterine volume), we did not observe a significant increase in the odds of DD with increasing uterine volume (Table 4). We also evaluated fibroid location with respect to uterine axis as a potential predictor of DD. One hundred and sixty-five women had at least one fundal fibroid, and 72 had only nonfundal fibroids. We observed fundal fibroids to be somewhat more strongly associated with DD compared with nonfundal fibroids (aPOR_{fundal_fibroid} = 2.9 95% CI 1.4, 5.9 vs. aPOR_{nonfundal_fibroid} = 1.6 95% CI 0.9, 2.9). However, CIs overlapped between the two groups.

In the supplemental analysis, we found that the presence of pelvic pathology did not appear to significantly modify the association between fibroids and DD. The association between fibroids and DD among women without pelvic pathology present was aPOR = 1.7, and the association between fibroids and DD among women with pelvic pathology present was aPOR = 1.5 (P_{interaction} = 0.6).

Other factors associated with a significantly elevated odds of DD were parity, depression, younger age, and the presence of other pelvic pathology (Table 3). There was a 30% increased odds of DD for each delivery. Women with a history of depression had a twofold increased odds of having DD compared with women without a history of depression. Older premenopausal women were slightly less likely to have DD as compared with younger premenopausal women. As expected, women with pelvic pathology present had almost three times the odds of having DD as compared with women without pelvic pathology present.

Discussion

We found that fibroids were significantly associated with DD, aPOR = 1.7 (95% CI 1.09, 2.54), and that the association was stronger for severe DD. Compared with women without fibroids, those with fibroids had a threefold odds of having severe DD (DD that prevented normal activity “some” or “a lot”). We did not observe a dose response relationship between fibroids and DD in that increasing uterine volume did not appear to increase the odds of DD. Consistent with previous findings [9], fundal fibroids tended to be more strongly associated with DD than nonfundal fibroids. Other factors that were associated with an increased odds of DD included increasing number of deliveries, a history of depression, the presence of pelvic pathologic condition (i.e., endometriosis, prolapse), and younger age.

The association between DD and fibroids has not been well studied, and previous findings are mixed. Although there are anecdotal and case reports of dyspareunia being caused by fibroids [11], few epidemiologic studies have examined this association [7–9]. A small hospital-based case-control study that compared the prevalence and severity of DD between women undergoing surgery for other benign conditions with women with symptomatic fibroids found no difference in the prevalence and severity of DD among the comparison groups [7]. Lippman et al. conducted a cross-sectional analysis looking at the association between fibroids and pelvic pain including the presence of DD (population-based sample from the Seveso Women’s Health Study conducted in 1976) [9]. They found that women with fibroids were more likely to report mild and severe dyspareunia (OR_{mild} = 1.4, OR_{severe} 1.8). They measured DD severity by self-report of avoiding intercourse because of pain. Another hospital-based case-control study that compared fibroid symptoms

between women with sporadic fibroids ($n = 255$) and women with familial fibroids ($n = 45$) observed that women with familial fibroids had a higher prevalence of dyspareunia as compared with women with sporadic fibroids (43% vs. 28% P value = 0.01) [8]. They attributed the increase in pain symptoms to (i) an increased number of fibroids observed in the familial group as compared with the sporadic group and (ii) an increased expression of vasoactive substances such as vascular endothelial growth factor A found in heavier concentrations in fibroid tissue of familial fibroids as compared with sporadic fibroids (64% vs. 28%) [8]. Similar to our study, all the prior studies used cross-sectional data to evaluate the association. However, only one study used ultrasound screening to define fibroid status [9], and none of the prior studies adjusted for the number of deliveries which is likely to be a strong confounder in most populations.

Though we found that fibroids and DD were significantly associated, we did not find that the odds of DD increased with fibroid burden as measured by uterine volume. This is consistent with some [7,9], but not all, previous studies [8]. Several factors could have influenced this unexpected null finding. First, women with large symptomatic fibroids may be more likely to have had a prior hysterectomy, and women with surgical menopause were excluded from our study. Secondly, women with large symptomatic fibroids that cause dyspareunia may be more likely to abstain from intercourse as it may cause them too much discomfort, and these women were also excluded. Thus, it may be that we did not find a dose response relationship between fibroids and DD because of the exclusion of women with symptomatic fibroids who have either abstained from intercourse or have had a hysterectomy for their fibroids.

Interestingly, younger women were more likely to experience DD as compared with the rest of the sample. Genital sexual pain that includes both superficial and deep pain has also been reported as more frequent among young women [12]. Because we lack information on partner characteristics and the frequency and vigorousness of coitus, we are unable to consider these factors in relation to age of the participant. However, it is possible that younger women may have confounding factors such as more frequent coitus, which could help explain this finding.

Our study has important strengths. A major strength is that it is a large sample with participants randomly selected from membership in a

prepaid health plan. Another strength is that our study included large numbers of African American women who in general have a greater fibroid burden [13,14] but have been less studied. Importantly, our fibroid assessment relied on ultrasound screening, regardless of a prior clinical diagnosis. Fibroids often are not clinically diagnosed, so the ultrasound screening provided an unbiased determination of fibroid status. In addition, because of the extensive data collection effort and the large sample, we were better able than other studies to control for potential confounding factors such as number of deliveries.

There were also several weaknesses. As with the other studies, this is a cross-sectional data analysis, so we cannot determine causality. The association we observed between fibroids and DD could be because of shared causal pathways for the two conditions. Our questionnaire data assessing severe DD was based on self-reported responses to a series of symptom questions and did not involve clinical validation, nor did it take into consideration partner characteristics such as penis size which could contribute to DD severity. In addition, we only captured women who had such severe pain that it prevented them from normal activity. Pain scales that give a quantitative measure of pain (commonly used in a clinical setting) would also be informative. However, unlike some previously validated questionnaires, our DD questions do distinguish between pain felt deep inside and pain experienced at the vaginal introitus, which may have allowed us to better evaluate the association between fibroids and DD. Pain at the vaginal introitus during intercourse is likely to have different etiology such as atrophic vaginitis. Although it appears that women with DD often have concomitant vaginal pain at the introitus, this is not always the case as is demonstrated in this study (35% of women with DD also reported pain at the vaginal introitus Table 1).

In addition, our study, like most cross-sectional studies, is subject to selection bias. We excluded women who were not sexually active and women who did not complete our DD assessment. We did investigate possible bias from excluding those not having sex by examining their level of fibroid burden. If they were less likely to have fibroids than those included in the analysis, this could have removed a subset of fibroid-free women with DD, thus creating the observed association by selection bias. However, we found that those excluded because of not having sex had a higher prevalence of fibroids than those remaining in the analysis as

would be expected if fibroids were associated with such severe DD that some women did not have intercourse. Thus, selection bias from this exclusion cannot explain our findings. Furthermore, excluding women who have had a previous hysterectomy because of large symptomatic fibroids may have biased our dose response results toward the null as discussed above.

Like other published studies, we lacked data on some important confounders such as a history of sexual abuse, partner characteristics, and coital frequency. We used depression as a proxy for history of sexual abuse because depression can often be caused by a history of sexual abuse and trauma [15]. Partner characteristics and coital frequency may contribute to DD severity and explain why younger women have a slightly greater risk of DD as compared with older women.

Lippmann et al. reported a stronger association with DD for women who had fundally located fibroids [9]. Though we collected fibroid location data, it included only women with fibroids ≥ 2.0 cm diameter ($n = 536$). We also found that having at least one fundal fibroid among the evaluated fibroids was somewhat more strongly associated with having DD compared with having fibroids located only in the corpus or below. A possible explanation for why fundal fibroids might be linked with DD is that fundal fibroids might induce uterine retroversion of the uterus, which might affect pain. We had data on whether a uterus was retroverted, and when we examined that factor, we found no association with DD $aPOR_{\text{retroverted}} = 1.1$ (95% CI 0.64, 2.03). Another possible explanation for the importance of fundal fibroids is that they are anatomically furthest away from the perforating branches of the uterine artery that enters the uterus bilaterally near the cervico-uterine junction [16,17]. Furthermore, the architecture of the smooth muscle fibers change as one descends caudally from the fundus to the cervix. Criss-crossing longitudinal and oblique smooth muscle fibers are more abundant in the fundus and corpus, whereas circular smooth muscle fibers are more abundant in the cervix [18]. The criss-crossing smooth muscle fibers higher up in the uterine myometrium are much more efficient at constricting blood vessels than the musculature lower down near and in the cervix [18]. Thus, fundal fibroids may be more prone to chronic devascularization and ischemic infarction. Other mechanisms that may lead to pain with fundal fibroids include inflammatory pathways relating to alternating periods of cell proliferation and cell death, but these processes have

been hypothesized for fibroid tumorigenesis in general, not just for fundal fibroids [19,20].

Another potential mechanism of action through which fibroids may cause pain during intercourse is by interfering with physiologic responses that facilitate normal conditions of intercourse. Fibroids might interfere with orgasm (which is characterized by contractions of the uterus, cervix, and vaginal musculature) or with tenting and cervical elevation during intercourse, which results in vaginal elongation and “ballooning” of the upper third of the vagina (a common physiologic occurrence during the arousal phase of the female sexual cycle) [21].

Delivery of a child has been shown to impact sexual functioning for women [22,23]. Although many factors are most likely leading to an overall decline in sexual functioning surrounding childbirth, one factor (perineal injury) may be specifically linked to the development of DD. Some studies have observed that dyspareunia for many women improves by 6–12 months after childbirth regardless of the mode of delivery [23,24]; other studies have shown that persistent dyspareunia after childbirth is linked to more severe tearing and or assisted vaginal deliveries [25–27]. Although we did not distinguish between the modes of delivery in this study, we did observe that the number of deliveries was positively associated with the odds of having DD, $aPOR = 1.3$ (95% CI 1.1, 1.5).

Many barriers exist when addressing issues of sexual dysfunction. It is often multifactorial, patients are reluctant to discuss this issue, sparse treatment options are available, and it often requires a multidisciplinary approach. However, its significant impact on women has become more apparent [28]. Our study that showed that women with fibroids are more likely to have dyspareunia than those without fibroids indicates that at the time of a fibroid diagnosis, physicians might easily introduce questions about sexual function. Prospective data are needed to show whether fibroids can actually cause or exacerbate dyspareunia.

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