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Influence of Body Size and Body Fat Distribution on Risk of Uterine Leiomyomata in U.S. Black Women

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Abstract

Background—Uterine leiomyomata are a major source of morbidity in black women. We prospectively investigated the risk of self-reported uterine leiomyomata in relation to body mass index (BMI), weight change, height, waist and hip circumferences, and waist-to-hip ratio in a large cohort of U.S black women.

Methods—Data were derived from the Black Women's Health Study, a U.S. prospective cohort study of black women who complete biannual mailed health questionnaires. From 1997 through 2001, we followed 21,506 premenopausal women with intact uteri and no prior diagnosis of uterine leiomyomata. Cox regression models were used to estimate incidence rate ratios (IRRs) and 95% confidence intervals (CIs).

Results—After 70,345 person-years of follow up, 2146 new cases of uterine leiomyomata confirmed by ultrasound (n = 1885) or hysterectomy (n = 261) were self-reported. Compared with the thinnest women (BMI <20.0 kg/m^2), the multivariate IRRs for women with BMIs of 20.0–22.4, 22.5–24.9, 25.0–27.4, 27.5–29.9, 30.0–32.4, and 32.5= kg/m^2 were 1.34 (95% CI = 1.02–1.75), 1.39 (1.07–1.81), 1.45 (1.12–1.89), 1.47 (1.11–1.93), 1.36 (1.02–1.80), and 1.21 (0.93–1.58), respectively. IRRs were larger among parous women. Weight gain since age 18 was positively associated with risk, but only among parous women. No other anthropometric measures were associated with risk.

Conclusions—BMI and weight gain exhibited a complex relation with risk of uterine leiomyomata in the Black Women's Health Study. The BMI association was inverse J-shaped and findings were stronger in parous women. Weight gain was positively associated with risk among parous women only.

Uterine leiomyomata (fibroids) are benign neoplasms arising from smooth muscle of the uterus and are the leading cause of hysterectomy in the United States.[1] Symptoms can include heavy

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menstrual bleeding, pelvic pain, and reproductive dysfunction.[2,3] Black women have 2 to 3 times the risk of white women,[3,4] as well as earlier ages at first diagnosis[2–4] and more numerous and symptomatic tumors at the time of diagnosis.[2,3]

Ovarian hormones are believed to play a key role in the etiology of uterine leiomyomata.[5] Body mass index (BMI = weight[kg]/height[m]^2) is a measure of absolute body fat[6] and may influence the risk of uterine leiomyomata through changes in steroid hormone metabolism and bioavailability.[7] Studies in premenopausal women have consistently documented an inverse association between BMI and circulating levels of sex hormone-binding globulin.[8–10] Decreases in sex hormone-binding globulin may increase the proportion of free estrogen or the fraction available for biologic activity.[8] Obesity is associated with diminished 2-hydroxylation of estrone to catechol estrogens and increased 16-alpha-hydroxylation of estrone to estriol, thereby producing estrogens with greater uterotropic activity.[11,12]

Epidemiologic studies of predominantly white populations show mixed results with respect to the association between BMI and uterine leiomyomata.[13–17] Although some studies show a positive association[13,15,16] or an inverse J-shaped association,[14,17] others show no association.[18–20] One of these studies[15] also found a positive association with adult weight gain, but not with height or BMI at age 18. There is evidence that premenopausal black women may have higher ovarian hormone levels than white women[21,22] and that estradiol levels decrease with increasing BMI in black women, but not white women.[23] Given these observations, the influence of BMI on risk of uterine leiomyomata may differ between black and white women.

The relation of uterine leiomyomata to body fat distribution, as measured by waist circumference or waist-to-hip ratio,[6] has not been evaluated. Independent of BMI, central obesity (excess fat in the upper trunk region) is associated with hormonal and metabolic changes in premenopausal women,[24] including altered estrogen metabolism,[24] insulin resistance and hyperinsulinemia,[25,26] and decreases in sex hormone-binding globulin levels.[9,24] Insulin, which is itself a mitogenic agent,[5] is associated with downregulation of sex hormone-binding globulin[26] and upregulation of insulin-like growth factor-1 and epidermal growth factor[5]; these agents could influence tumor development through direct promotion of myometrial smooth muscle cell proliferation or enhanced ovarian hormone secretion.[5,7]

In the United States, the prevalence of obesity (BMI $\geq$30 kg/m^2) is nearly twice as high in black women as in white women.[27] If obesity is related to an increased risk of uterine leiomyomata, obesity might explain a large fraction of the disease burden among black women. We prospectively investigated the influence of BMI and other anthropometric measures—weight gain, height, waist circumference, and waist-to-hip ratio—on risk of uterine leiomyomata in pre-menopausal U.S. black women.

METHODS

Study Population

The Black Women's Health Study is an ongoing prospective cohort study of risk factors for major illnesses in U.S. black women. Approximately 59,000 black women age 21 to 69 years were enrolled through questionnaires mailed mainly to subscribers of *Essence* magazine and have been followed since March 1995.[28] The baseline questionnaire elicited information on demographic and behavioral characteristics, reproductive and contraceptive histories, healthcare utilization, and medical conditions. Updated information is obtained by mailed questionnaire every 2 years and more than 80% of the cohort has completed a questionnaire in each follow-up cycle. Respondents represent various geographic regions of the United

States, with the majority residing in California, New York, Illinois, Michigan, Georgia, and New Jersey.

Follow up for the present analysis began in 1997, the start of the second questionnaire cycle, because data on method of confirmation for uterine leiomyomata were first obtained on the 1999 questionnaire. Of the 53,322 women who completed the 1997 questionnaire, we restricted the analytic sample to premenopausal women with intact uteri (n = 36,618), because uterine leiomyomata are rare after menopause.[4,13,17] We excluded women who reported a diagnosis of leiomyomata before 1997 (n = 10,449), who did not complete a 1999 or a 2001 follow-up questionnaire (n = 2307), "cases" with no information about year of diagnosis (n = 100) or confirmation method (n = 207), and women with potentially unrepresentative anthropometric measurements (those who were currently pregnant at the time they completed the 1995 [n = 566] or 1997 [n = 392] questionnaires; who reported gastric surgery for weight loss [n = 55]; or who had implausible data on current weight, weight at age 18, height, or other covariates [n = 1059]). After these exclusions, 21,506 women remained and were followed over the subsequent 4 years. Separate analyses were conducted for women with complete data on waist and hip circumference (n = 17,876); these participants had a lower median BMI than those with incomplete data (26.0 vs. 27.3 kg/m^2).

Assessment of Uterine Leiomyomata

Transvaginal ultrasound is the clinical standard used to confirm diagnoses of uterine leiomyomata. Although histologic evidence is the gold standard,[29] histologically confirmed cases represent only 10% to 30% of cases for whom ultrasound evidence is available.[4,7] Studies limited to histologic cases may spuriously identify risk factors associated with large tumor size, symptoms, or treatment preference.[7] To minimize the potential for bias, we expanded our outcome definition to include confirmation by ultrasound and/or hysterectomy. This definition was previously used by the Nurses' Health Study II, a prospective study with similar methodology.[4,15] Ultrasound has high sensitivity (99%) and specificity (91%) relative to histologic evidence.[29]

On the 1999 and 2001 follow-up questionnaires, women were asked if they had been diagnosed with "fibroids" in the previous 2-year interval and, if "yes," the calendar year in which they were first diagnosed and the method of confirmation: "pelvic examination" or "ultrasound/ hysterectomy." A diagnosis was classified as "hysterectomy-confirmed" if the woman reported hysterectomy on the same questionnaire.

Incident cases were defined as women who self-reported on the 1999 or 2001 questionnaire a *first* diagnosis of "fibroids" confirmed by ultrasound or hysterectomy. The index date for each case was defined as the midpoint of the reported calendar year in which the diagnosis was confirmed. Women with diagnoses confirmed only by pelvic examination (n = 387) were treated as noncases in primary analyses because their diagnoses may have represented other pathology.[15,29] As the diagnosis may have influenced a change in lifestyle factors, their exposure information was not updated beyond the time of diagnosis.

We assessed the accuracy of self-reported uterine leiomyomata in a random sample of 248 cases confirmed by ultrasound or hysterectomy. These women were mailed supplemental questionnaires regarding symptoms, diagnostic confirmation, and treatment, and were asked for permission to review their medical records. We obtained medical records for 127 of the 128 women who gave us permission, and we confirmed the self-report in 122 (96%). The proportion of cases reporting an initial diagnosis confirmed by ultrasound varied little with BMI, ranging from 100% among the leaner women (BMI <20 kg/m^2) to 96% among the obese women (BMI ≥30 kg/m^2). Among the 188 (76%) cases who completed the supplemental

questionnaire, 71% reported the presence of symptoms before diagnosis; this proportion was similar across categories of BMI.

Assessment of Body Size, Body Fat Distribution, and Other Covariates

In 1995, we collected information on self-reported height (feet and inches), current weight (pounds), weight at age 18 (pounds), waist circumference (inches) at the level of the umbilicus, and hip circumference (inches) at its widest location. Current weight was updated every 2 years by follow-up questionnaire. BMI was calculated as weight (kg) divided by height squared (m^2).

In 2001, Howard University investigators conducted a validation study of anthropometric measures among Black Women's Health Study participants from the Washington, DC, area. The first 115 participants who responded to mailed invitations were enrolled. The Spearman correlation between self-reported weight (mean = 176 lbs) and technician-measured weight (mean = 181 lbs) was 0.97. The coefficient between self-reported height (mean = 64.4 in) and technician-measured height (mean = 64.0 in) was 0.93. Spearman correlations for self-reported versus technician-measured waist circumference, hip circumference, and waist-to-hip ratio were 0.75, 0.74, and 0.54, respectively. Self-reported waist, hip, and waist-to-hip ratio measurements were, on average, 4.7 inches, 3.1 inches, and 0.05 units lower than technician measurements.

Data on parity, age at each birth, oral contraceptives, smoking, and alcohol consumption were obtained on the baseline and follow-up questionnaires, and were treated as time-dependent variables in the analysis, as were BMI and weight gain.

Data Analysis

Each participant contributed person-time from March 1997 until the diagnosis of uterine leiomyomata, menopause, death, loss to follow up, or March 2001 (end of follow up), whichever came first. Incidence rates (IRs) in each category of the exposure variable were computed by dividing the number of incident cases in that category by the person-time in that category. We used multivariate Cox regression to estimate incidence rate ratios (IRRs) and 95% confidence intervals (CIs) for anthropometric variables of interest. To control for age, calendar time, and any 2-way interactions between these 2 time scales, we stratified our analyses jointly by baseline age in 1-year intervals and calendar year of the current questionnaire cycle.

A covariate was included in multivariate analyses if the literature supported its role as a confounder, or if adding it to a model containing all other risk factors for uterine leiomyomata changed the exposure IRR by 10% or more.[30] Based on these criteria, we controlled for age at menarche, parity, age at first birth, years since last birth, oral contraceptive use, smoking, alcohol consumption, education, and geographic region.

Because parous women have a lower risk of uterine leiomyomata than nulliparous women,[7,31] and are more likely to gain weight[32,33] and have central obesity,[33] we stratified the analyses by parity status. To examine whether the main associations were modified by parity or other risk factors, we conducted likelihood ratio tests that compared models with and without crossproduct terms between anthropometric variables (categorical) and selected covariates. Departures from the proportional hazards assumption (ie, effect modification by age and time) were tested by the likelihood ratio test comparing models with and without crossproduct terms between anthropometric variables and both time period (1997–1999 vs. 1999–2001) and age (<35 vs. 35+).

RESULTS

At the start of follow up (1997), 29% of the cohort was overweight (BMI = 25–29 kg/m^2) and 30% was obese (BMI ≥30 kg/m^2) according to World Health Organization standards[34] (Table 1). Current BMI was positively related to BMI at age 18 years, waist circumference, hip circumference, parity, years since last birth, and energy intake, and inversely related to height, age at menarche, age at first birth, smoking, alcohol intake, and vigorous physical activity. Women living in the West were less likely than those living in other geographic regions to be overweight. Results from the Black Women's Health Study regarding risk of uterine leiomyomata in relation to age,[35] reproductive factors,[31] and alcohol, caffeine, and tobacco consumption[36] have been published elsewhere.

During 70,345 person-years of follow up, 2146 new cases of uterine leiomyomata confirmed by ultrasound (n = 1885) or hysterectomy (n = 261) were self-reported. Compared with BMI <20.0 kg/m^2, multivariate IRRs were elevated in all categories of BMI and ranged from 1.21 to 1.47 (Table 2). IRRs were larger among parous than nulliparous women (*P* value, test for interaction = 0.002). Crude incidence rates were higher in nulliparous women than in parous women, but only among women with normal or low BMI (Table 2). Associations in both groups were inverse J-shaped, although the peak incidence in risk differed: BMI = 27.5–29.9 kg/m^2 in parous women versus BMI = 22.5–24.9 kg/m^2 in nulliparous women. At the start of follow up, obese nulliparous women could have been more likely to have ovulatory infertility[37] and less likely to have incident tumors detected by pregnancy ultrasound than lean nulliparous women. However, the same pattern of risk emerged after the exclusion of nulliparous women who reported infertility in 1995 or who reported a subsequent livebirth within the same 2-year interval as their diagnosis.

Multivariate IRRs for BMI at age 18 were not notably different from 1.0 and did not vary appreciably by parity (Table 2). A positive association between weight gain since age 18 and uterine leiomyomata was evident among parous but not nulliparous women (*P* value, test for interaction <0.001). Among parous women, the multivariate IRR comparing weight gain of 25 + to <5 kg was 1.54 (95% CI = 1.21–1.98) and a positive monotonic trend was observed. Crude incidence rates were notably higher among nulliparous women than among parous women, but only in the lowest categories of weight gain. Adult height was not associated with risk.

None of the body fat distribution measures was independently associated with risk of uterine leiomyomata overall or among parity subgroups (Table 2). Findings remained unchanged when we controlled for height, BMI at age 18, or waist and hip circumference. In addition, no associations were found within subgroups of adult BMI (data not shown).

In analyses confined to hysterectomy-confirmed cases only, overall findings for anthropometric variables were similar to those in the combined group of cases (Table 3). The IRRs for BMI were larger than those derived from analyses among all cases, but the same inverse J-shaped pattern was observed. The IRRs for weight gain were stronger than the overall analyses. Because over 80% of hysterectomy-confirmed cases were parous, small numbers precluded the assessment of interaction.

The overrepresentation of hysterectomy-confirmed cases among parous cases (19%) relative to nulliparous cases (5%) could have contributed to the observed parity interaction because associations were stronger in hysterectomy-confirmed cases. However, when we repeated the analyses among ultrasound-confirmed cases only (data not shown), the parity interaction with BMI and weight gain remained (*P* values = 0.01 and 0.005, respectively). The parity interaction also persisted within subgroups of age (<35 vs. 35+).

Because obese women were less likely than women of normal weight to report a recent Papanicolaou smear (Table 1), a marker of pelvic examination, we restricted analyses to the 90% of women who reported this practice. None of the results changed materially. In addition, results were similar when cases confirmed by pelvic examination (N = 387) were included as part of the outcome definition, censored at the time of diagnosis, or excluded at baseline. Finally, we found no evidence of effect modification by age, education, smoking, and geographic region, risk factors by which study participants may differ from other U.S. black women.

DISCUSSION

The present study is the largest prospective examination of anthropometric risk factors for uterine leiomyomata in U.S. black women. Overall findings for BMI and risk of uterine leiomyomata showed an inverse J-shaped pattern, with elevated IRRs for all categories of BMI above 20.0 kg/m^2 and a peak incidence associated with a BMI category of 27.5–29.9 kg/m^2. These results are consistent with previous studies that found a positive[13,15,16] or inverse J-shaped association,[14,17] but not with 3 other studies that found no association,[18–20] including one that stratified by race.[20]

The Nurses' Health Study II, which has similar methodology to our study but includes >95% white women, observed similar associations for BMI.[15] Multivariate IRRs increased with increasing BMI categories until reaching a peak at BMI 28.0–29.9 kg/m^2, after which the risk decreased slightly.[15] If BMI <20.0 kg/m^2 were the reference category, the resulting IRR would have been 1.51, which is similar to the peak IRR observed in our data (1.47 for BMI = 27.5–29.9 kg/m^2); however, the difference in risk between the normal and overweight BMI categories was less pronounced in our study than in the Nurses' Health Study II. Like in the Nurses' Health Study II, we found stronger associations among hysterectomy-confirmed cases. These data suggest that higher BMI might be associated with greater symptomatology. We remain cautious about the interpretation of results for hysterectomy-confirmed cases because numbers are small and the IRRs are more likely to reflect bias.[7]

The inverse J-shaped pattern for BMI and risk of uterine leiomyomata was present within parity subgroups and remained evident after the exclusion of nulliparous women who reported infertility, women who had a livebirth in a subsequent time interval, and women without a recent Papanicolaou smear. The observed pattern might be a real biologic phenomenon explained by decreased menstrual cycling among excessively thin and obese women compared with normal-weight women.[37] A decrease in menstrual cyclicity may reduce risk of uterine leiomyomata by lowering levels of circulating estrogens and progesterone. Conversely, the observed pattern could reflect a detection bias if, for example, clinicians had greater difficulty detecting tumors by pelvic examination in obese women.

Our data suggest that the influence of elevated adult BMI and weight gain is greater among parous than nulliparous women. Epidemiologic studies show that parous women are at lower risk of uterine leiomyomata than nulliparous women, which may be the result of the long-term parity-related reduction in hormones associated with myoma growth such as estradiol and prolactin.[38,39] Absolute incidence rates were higher in nulliparous women than in parous women, but only among women with normal or low BMI (or <25-kg weight gain), suggesting that overweight or obesity may dampen the protective effect of parity.[31] The greater relative increase in exposure to endogenous hormones might explain how parity modifies the effect of BMI. For example, estrogens derived from adipose tissue may have a larger impact on parous women because their mean endogenous estrogen levels are significantly lower than those of nulliparous women.[39]

Differential exclusions could have created the appearance of interaction by parity in the relationship between BMI/weight gain and uterine leiomyomata. More than 10,000 women with a previous diagnosis of uterine leiomyomata were excluded before baseline. Although the current standard of clinical detection is transvaginal ultrasound, prior diagnoses could have depended on a wide array of diagnostic techniques with lower sensitivity in obese women (eg, pelvic examination or transabdominal ultrasound). Before baseline, most parous women will have had a pregnancy ultrasound during which tumors, if present, could have been identified. However, if this prestudy pregnancy screening were more effective in lean women, the study population at baseline could have disproportionately included obese women with undetected tumors. Consequently, transvaginal ultrasound might have picked up these undetected tumors in our study and overestimated the effect of obesity among parous women. Therefore, the observed parity interaction warrants confirmation in future studies.

Although height is associated with higher follicular-phase plasma estradiol levels in premenopausal women,[8] we found no evidence of an association between height and uterine leiomyomata, consistent with findings from the Nurses' Health Study II.[15] Likewise, the null association found for BMI at age 18 agrees with Nurses' Health Study II results.[15]

The influence of body fat distribution on risk of uterine leiomyomata has not been previously evaluated. Several studies have documented that central obesity is greater for black women than white women[40] and is positively associated with age[40] and parity.[33] Neither waist circumference nor waist-to-hip ratio was associated with risk of uterine leiomyomata in the present study. Although our validation data showed that lean women reported waist-to-hip ratio with greater accuracy than obese women (Pearson correlation: 0.52 vs. 0.23), null associations were found in both groups. A combination of several counteracting effects could explain the lack of association. Although there is evidence that women with greater upper body obesity have decreased sex hormone-binding globulin levels,[9,24] altered estrogen metabolism,[24] and hyperinsulinemia,[25,26] factors that may promote tumor development, there is also evidence that upper body obesity is associated with anovulation,[25] which may reduce the risk of uterine leiomyomata.[31]

Validation data on weight and height showed strong correlations between self-reported and technician measurements. Correlations were lower for waist circumference, hip circumference, and waist-to-hip ratio. Because anthropometric data were collected before the diagnosis and confirmation of uterine leiomyomata, error in self-reported anthropometric measures was likely nondifferential. When there are several categories of exposure, nondifferential misclassification can bias results toward or away from the null.[30]

Study participants were not systematically screened for uterine leiomyomata. As a result of the high cumulative incidence of these tumors and their tendency to be asymptomatic,[3] true cases may have been misclassified as noncases. In a study that screened randomly selected women age 35–49 years from an urban health plan, 59% of premenopausal black women reporting no previous diagnosis of uterine leiomyomata showed ultrasound evidence of the condition,[3] although many of the tumors were not clinically significant. Because specificity of disease classification was high in our study, as indicated by the low proportion of false-positive diagnoses (4%), we expect little bias resulting from nondifferential misclassification.[30] Bias resulting from differential disease misclassification is more likely because BMI can affect healthcare use, which can influence the probability of fibroid detection. Although lower levels of screening among obese women (Table 1) could have produced a downward bias of the BMI association, results were similar when we restricted the analytic sample to the 90% of women who reported a recent Papanicolaou smear.

High follow up in our study reduces the potential for selection bias. However, subscribers to *Essence* magazine may differ from the general population of U.S. black women in ways that may affect the generalizability of our findings to the larger population. The distributions of BMI and parity in our cohort were similar to those documented in nationally representative studies of reproductive-aged black women.[27,41] Moreover, we did not find any effect modification by education, smoking, or geographic region on the main associations. Therefore, we expect the present findings to extend to other U.S. black women.

The associations of uterine leiomyomata with BMI and weight gain in the present study are too complex to support simple recommendations for the prevention of uterine leiomyomata. Women in the normal range of BMI might decrease their risk with weight loss, but the opposite effect might hold true for obese women. The consistent finding of a reduced risk among the leanest women (BMI <20 kg/m^2) supports the hypothesis that uterine leiomyomata are hormone-dependent tumors.[5] A variety of hormones may be involved in this modification of risk, given that thin or anorexic women are found to have higher levels of sex hormone-binding globulin,[8,9] decreased prolactin secretion,[42] and increased hydroxylation of estrone to catechol estrogens[11]—all of which may create an endogenous hormonal milieu with lower susceptibility to uterine leiomyomata.

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TABLE 1

Characteristics of 21,506 Premenopausal Women According to Body Mass Index (kg/m^2): the Black Women's Health Study, 1997*

Characteristic	Body Mass Index			
	<20.0 (n = 1330)	20.0–24.9 (n = 7454)	25.0–29.9 (n = 6336)	30.0+ (n = 6386)
BMI (kg/m^2); mean	18.9	22.7	27.3	36.4
BMI at age 18 yr (kg/m^2); mean	17.8	19.8	21.5	25.4
Height (1995) (in); mean	65.6	65.1	65.1	64.9
Waist circumference (1995) (in); mean†	25.8	28.2	31.5	36.9
Hip circumference (1995) (in); mean†	34.2	37.0	40.1	45.2
Energy intake (1995) (kcal/d); mean‡	1540	1450	1522	1664
Age at menarche (yr); mean§	13.1	12.6	12.3	12.0
Age at first birth (yr); mean§	23.8	23.5	22.9	22.4
Time since last birth (yr); mean§	10.1	10.4	10.5	11.0
Age (yr); %				
<30	45	32	23	23
30–39	43	45	45	44
40+	12	23	32	33
Parous; %	51	54	58	58
Geographic region of residence (1995); %				
Northeast	30	28	28	29
West	21	21	18	15
Midwest	20	21	23	25
South	29	30	31	31
Education (1995) (yrs); %				
≤ 12	11	10	14	17
13–16	66	65	65	65
17+	23	25	21	18
Papanicolaou smear since 1995; %	89	92	91	88
Oral contraceptive use; %				
Current user	23	27	24	18
Former user	56	56	58	60
Cigarette smoking; %				
Current smoker	17	13	14	15
Former smoker	9	12	14	16
Current alcohol intake (1+ drinks/wk); %	27	29	29	25
Vigorous physical activity; %				
None	41	31	36	49
<5 h/wk	48	54	53	45
5+ h/wk	11	15	11	6

* Data from 1997 (start of follow up) unless otherwise noted. Characteristics (with exception of age) are standardized to age distribution of women free of uterine leiomyomata at the start of follow up.

† Limited to 17,876 women with complete data on waist and hip circumference.

‡ Limited to 20,020 women with complete data on energy intake derived from a self-administered 68-item Block food frequency questionnaire.

§ Limited to 12,022 parous women.

TABLE 2

Incidence Rates (IRs) per 1000 Person-Years and Incidence Rate Ratios (IRRs) for Uterine Leiomyomata Confirmed by Ultrasound or Hysterectomy According to Measures of Body Size and Body Fat Distribution

Anthropometric Variable	All Women				Parous Women			Nulliparous Women			*P* Value, Test for Interaction†
	No. of Cases	Person-Years	Crude IR	Multivariate IRR (95% CI)*	No. of Cases	Crude IR	Multivariate IRR (95% CI)*	No. of Cases	Crude IR	Multivariate IRR (95% CI)*	
BMI, current (kg/m^2)											0.002
<20.0	80	4033	19.8	1.00‡	27	16.1	1.00‡	53	22.5	1.00‡	
20.0–22.4	290	10,297	28.2	1.34 (1.02–1.75)	109	22.3	1.26 (0.78–2.01)	181	33.5	1.46 (1.04–2.04)	
22.5–24.9	419	13,297	31.5	1.39 (1.07–1.81)	192	26.3	1.41 (0.90–2.22)	227	37.8	1.46 (1.04–2.03)	
25.0–27.4	423	12,606	33.6	1.45 (1.12–1.89)	237	30.9	1.66 (1.06–2.59)	186	37.7	1.38 (0.98–1.93)	
27.5–29.9	267	8085	33.0	1.47 (1.11–1.93)	167	33.7	1.81 (1.15–2.86)	100	31.9	1.23 (0.85–1.77)	
30.0–32.4	218	6778	32.2	1.36 (1.02–1.80)	129	31.3	1.70 (1.07–2.70)	89	33.4	1.14 (0.78–1.66)	
32.5+	449	15,250	29.4	1.21 (0.93–1.58)	269	30.2	1.48 (0.95–2.32)	180	28.4	1.04 (0.74–1.47)	
BMI at age 18 (kg/m^2)											0.98
<18.5	386	12,500	30.9	1.00‡	220	28.7	1.00‡	166	34.4	1.00‡	
18.5–19.9	421	13,877	30.3	1.02 (0.88–1.18)	230	27.9	1.06 (0.87–1.29)	191	33.9	0.98 (0.78–1.23)	
20.0–22.4	693	21,104	32.8	1.08 (0.95–1.24)	366	30.4	1.14 (0.95–1.37)	327	36.0	1.01 (0.82–1.24)	
22.5–24.9	341	10,899	31.3	1.02 (0.87–1.20)	175	28.9	1.07 (0.86–1.33)	166	34.3	0.98 (0.77–1.24)	
25.0–27.4	154	5884	26.2	0.90 (0.73–1.09)	79	26.8	1.02 (0.77–1.35)	75	25.6	0.78 (0.58–1.04)	
27.5–29.9	66	2469	26.7	0.88 (0.66–1.16)	30	25.9	0.94 (0.61–1.43)	36	27.5	0.82 (0.56–1.21)	
30.0+	85	3613	23.5	0.81 (0.62–1.04)	30	21.5	0.86 (0.57–1.29)	55	24.8	0.76 (0.54–1.05)	
Weight gain since age 18 (kg)											<0.001
<5	325	12,900	28.2	1.00‡	104	19.8	1.00‡	221	28.9	1.00‡	
5–9	312	10,994	28.4	1.10 (0.93–1.30)	120	22.7	1.21 (0.90–1.61)	192	33.6	1.04 (0.85–1.29)	
10–14	372	12,021	30.9	1.13 (0.97–1.33)	183	26.9	1.44 (1.10–1.88)	189	36.3	1.01 (0.81–1.25)	
15–24	595	18,016	33.0	1.18 (1.01–1.36)	356	31.0	1.45 (1.13–1.86)	239	36.6	1.05 (0.86–1.28)	
25+	542	16,414	33.0	1.10 (0.95–1.29)	367	34.4	1.54 (1.21–1.98)	175	30.5	0.81 (0.65–1.00)	
Height (feet and inches)											0.95
≤5′ 2″	368	12,709	29.0	1.00‡	199	26.6	1.00‡	169	32.4	1.00‡	
5′ 3″–5′ 4″	539	17,721	30.4	1.04 (0.90–1.19)	287	28.2	1.06 (0.87–1.29)	252	33.4	1.02 (0.83–1.26)	
5′ 5″–5′ 6″	620	18,872	32.9	1.17 (1.02–1.34)	335	31.0	1.23 (1.02–1.48)	285	35.3	1.10 (0.89–1.34)	
5′ 7″–5′ 8″	385	13,397	28.7	1.04 (0.89–1.21)	201	27.8	1.14 (0.92–1.41)	184	29.9	0.94 (0.75–1.18)	
5′ 9″+	234	7647	30.6	1.08 (0.90–1.29)	108	28.5	1.17 (0.90–1.50)	126	32.7	1.01 (0.79–1.30)	
Waist circumference (inches)§											0.10

Anthropometric Variable	All Women				Parous Women			Nulliparous Women			*P* Value, Test for Interaction[†]
	No. of Cases	Person-Years	Crude IR	Multivariate IRR (95% CI)[*]	No. of Cases	Crude IR	Multivariate IRR (95% CI)[*]	No. of Cases	Crude IR	Multivariate IRR (95% CI)[*]	
<27	284	10,317	27.5	1.00[‡]	115	24.3	1.00[‡]	169	30.3	1.00[‡]	
27–29	452	14,146	32.0	1.08 (0.92–1.28)	193	26.8	1.00 (0.77–1.29)	259	37.3	1.16 (0.93–1.45)	
30–32	403	12,951	31.1	1.01 (0.84–1.21)	237	30.3	1.02 (0.78–1.33)	166	32.4	1.01 (0.78–1.31)	
33–35	286	8182	35.0	1.16 (0.94–1.43)	171	33.7	1.14 (0.85–1.52)	115	37.0	1.21 (0.89–1.66)	
36+	377	12,938	29.1	0.97 (0.77–1.21)	226	28.9	0.97 (0.71–1.33)	151	29.6	0.99 (0.71–1.39)	
Hip circumference (inches)[§]											0.15
<36	278	10,226	27.2	1.00[‡]	120	23.8	1.00[‡]	158	30.5	1.00[‡]	
36–37	315	10,198	30.9	1.11 (0.93–1.32)	147	27.2	1.18 (0.90–1.53)	168	35.1	1.04 (0.82–1.32)	
38–40	474	14,869	31.9	1.04 (0.87–1.24)	257	29.9	1.14 (0.88–1.47)	217	34.6	0.96 (0.75–1.22)	
41–44	408	12,779	31.9	1.04 (0.85–1.26)	236	30.7	1.08 (0.82–1.43)	172	33.8	1.01 (0.76–1.34)	
45+	327	10,463	31.3	1.10 (0.88–1.38)	182	30.7	1.23 (0.90–1.67)	145	32.0	0.97 (0.69–1.36)	
Waist-to-hip ratio[§]											0.50
<0.71	349	11,838	29.5	1.00[‡]	153	25.5	1.00[‡]	196	33.6	1.00[‡]	
0.71–0.75	375	11,611	32.3	1.07 (0.92–1.25)	187	30.9	1.12 (0.89–1.42)	188	33.8	1.02 (0.82–1.27)	
0.76–0.79	385	11,993	32.1	1.11 (0.95–1.30)	198	29.6	1.09 (0.87–1.37)	187	35.2	1.12 (0.90–1.39)	
0.80–0.85	368	11,521	31.9	1.12 (0.95–1.31)	217	32.3	1.23 (0.98–1.54)	151	31.6	1.03 (0.81–1.30)	
0.86+	325	11,571	28.1	0.98 (0.83–1.16)	187	25.9	0.93 (0.73–1.18)	138	31.7	1.10 (0.86–1.41)	

[*] Adjusted for age (1-yr intervals), time period (1997–1999 vs. 1999–2001), age at menarche (years), parity (number of births), age at first birth (years), years since last birth (linear term + 2 spline terms), ever use of oral contraceptives, education (≤12, 13–15, 16, 17+), living in the West, current alcohol consumption (<1, 1–6, 7+ per week), and smoking (never, former, current). Models of waist, hip, and waist-to-hip ratio measures are further adjusted for BMI in 1995 (<20, 20–24, 25–29, 30+).

[†] Likelihood ratio test comparing models with and without categorical anthropometric variable by parity interaction terms.

[‡] Reference category.

[§] Limited to 17,876 women with complete data on waist and hip circumference in 1995.

TABLE 3

Incidence Rates per 1000 Person-Years and Rate Ratios for Uterine Leiomyomata Confirmed by Hysterectomy According to Measures of Body Size and Body Fat Distribution

Anthropometric Variable	No. of Cases	Person-Years	Crude IR	Multivariate IRR (95% CI)*
BMI, current (kg/m^2)				
<20.0	3	4033	0.7	1.00†
20.0–22.4	22	10,297	2.1	2.22 (0.66–7.45)
22.5–24.9	44	13,297	3.3	2.90 (0.90–9.37)
25.0–27.4	54	12,606	4.3	3.20 (1.00–10.29)
27.5–29.9	42	8085	5.2	3.73 (1.15–12.09)
30.0–32.4	37	6778	5.5	3.73 (1.14–12.17)
32.5+	59	15,250	3.9	2.67 (0.83–8.57)
BMI at age 18 (kg/m^2)				
<18.5	52	12,500	4.2	1.00†
18.5–19.9	54	13,877	3.9	1.02 (0.69–1.49)
20.0–22.4	87	21,104	4.1	1.13 (0.79–1.60)
22.5–24.9	41	10,899	3.8	1.08 (0.71–1.64)
25.0–27.4	15	5884	2.6	0.75 (0.42–1.34)
27.5–29.9	6	2469	2.4	0.76 (0.32–1.78)
30.0+	6	3613	1.7	0.58 (0.24–1.35)
Weight gain since age 18 (kg)				
<5	19	12,900	1.5	1.00†
5–9	21	10,994	1.9	1.06 (0.57–1.97)
10–14	48	12,021	4.0	1.93 (1.13–3.31)
15–24	83	18,016	4.6	1.79 (1.08–2.97)
25+	90	16,414	5.5	1.84 (1.11–3.05)
Height (feet and inches)				
≤5′2″	47	12,709	3.7	1.00†
5′3″–5′4″	60	17,721	3.4	0.95 (0.65–1.40)
5′5″–5′6″	78	18,872	4.1	1.19 (0.83–1.71)
5′7″–5′8″	53	13,397	4.0	1.26 (0.85–1.87)
5′9″+	23	7647	3.0	1.07 (0.64–1.77)
Waist circumference (inches)‡				
< 27	27	10,317	2.6	1.00†
27–29	37	14,146	2.6	0.73 (0.44–1.21)
30–32	64	12,951	4.9	1.02 (0.62–1.67)
33–35	38	8,182	4.6	0.85 (0.48–1.49)
36+	54	12,938	4.2	0.74 (0.41–1.34)
Hip circumference (inches)‡				
<36	23	10,226	2.2	1.00†
36–37	29	10,198	2.8	1.05 (0.60–1.83)
38–40	66	14,869	4.4	1.21 (0.73–1.99)
41–44	62	12,779	4.8	1.15 (0.67–1.98)
45+	40	10,463	3.8	0.92 (0.50–1.71)
Waist-to-hip ratio‡				
<0.71	39	11,838	3.3	1.00†
0.71–0.75	38	11,611	3.3	0.97 (0.62–1.51)
0.76–0.79	50	11,993	4.2	1.09 (0.71–1.66)
0.80–0.85	53	11,521	4.6	1.17 (0.77–1.78)
0.86+	40	11,571	3.5	0.83 (0.52–1.31)

*Adjusted for age (1-yr intervals), time period (1997–1999 vs. 1999–2001), age at menarche (years), parity (number of births), age at first birth (years), years since last birth (linear term + 2 spline terms), ever use of oral contraceptives, education (≤12, 13–15, 16, 17+), living in the West, current alcohol consumption (<1, 1–6, 7+ per week), and smoking (never, former, current). Models of waist, hip, and waist-to-hip ratio measures are further adjusted for BMI in 1995 (<20, 20–24, 25–29, 30+).

†Reference category.

‡Limited to 17,876 women with complete data on waist and hip circumference in 1995.