

## Original Contribution

# Hair Relaxer Use and Risk of Uterine Leiomyomata in African-American Women

Lauren A. Wise\*, Julie R. Palmer, David Reich, Yvette C. Cozier, and Lynn Rosenberg

\* Correspondence to Dr. Lauren A. Wise, Slone Epidemiology Center, Boston University, 1010 Commonwealth Avenue, Boston, MA 02215 (e-mail: lwise@bu.edu).

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Hair relaxers are used by millions of black women, possibly exposing them to various chemicals through scalp lesions and burns. In the Black Women's Health Study, the authors assessed hair relaxer use in relation to uterine leiomyomata incidence. In 1997, participants reported on hair relaxer use (age at first use, frequency, duration, number of burns, and type of formulation). From 1997 to 2009, 23,580 premenopausal women were followed for incident uterine leiomyomata. Multivariable Cox regression was used to estimate incidence rate ratios and 95% confidence intervals. During 199,991 person-years, 7,146 cases of uterine leiomyomata were reported as confirmed by ultrasound ( $n = 4,630$ ) or surgery ( $n = 2,516$ ). The incidence rate ratio comparing ever with never use of relaxers was 1.17 (95% confidence interval (CI): 1.06, 1.30). Positive trends were observed for frequency of use ( $P_{\text{trend}} < 0.001$ ), duration of use ( $P_{\text{trend}} = 0.015$ ), and number of burns ( $P_{\text{trend}} < 0.001$ ). Among long-term users ( $\geq 10$  years), the incidence rate ratios for frequency of use categories 3–4, 5–6, and  $\geq 7$  versus 1–2 times/year were 1.04 (95% CI: 0.92, 1.19), 1.12 (95% CI: 0.99, 1.27), and 1.15 (95% CI: 1.01, 1.31), respectively ( $P_{\text{trend}} = 0.002$ ). Risk was unrelated to age at first use or type of formulation. These findings raise the hypothesis that hair relaxer use increases uterine leiomyomata risk.

African Americans; female; hair straighteners; leiomyoma; prospective studies

Abbreviation: CI, confidence interval.

Uterine leiomyomata are tumors of the myometrium that are responsive to estrogens and progesterone. Although benign, uterine leiomyomata are associated with significant gynecologic morbidity and are the leading indication for hysterectomy in the United States (1, 2). The incidence of uterine leiomyomata is 2–3 times higher in US black women than in US white women (3, 4), and the lifetime risk of uterine leiomyomata—based on ultrasound evidence of pre-clinical and clinical disease—is estimated to be as high as 80% in US black women (4). The black-white disparity in uterine leiomyomata risk is not explained by established risk factors (3, 5).

Hair relaxers (straighteners) have been used by millions of US black women, often for long periods of time (6). Hair relaxers can cause burns and lesions in the scalp, facilitating entry of hair relaxer constituents into the body (7–14). The main ingredient of “lye” relaxers is sodium hydroxide; no-lye relaxers contain calcium hydroxide and guanidine carbonate, and “thio” relaxers contain thioglycolic acid salts (15). No-lye

relaxers are advertised to cause fewer scalp lesions and burns than lye relaxers, but there is little evidence to support this claim (16). Products may also contain hormonally active compounds (17), such as phthalates, which are not required to be listed separately as ingredients and are often reported under the term “fragrances” or “perfume” (18). Cosmetic products are not subject to premarket approval by the Food and Drug Administration, and a complete list of ingredients is not mandatory (19), making it unclear what types of chemicals they contain. However, because the vast majority of hair relaxers list “fragrance” as an ingredient, and 100% of popular fragrances tested in a 2002 study were found to contain phthalates (18, 20), most hair relaxers likely contain these chemicals. In addition, some hair relaxer products directly list phthalates as one of their chemical ingredients (21).

Phthalates from cosmetic products can be absorbed by the skin or inhaled (22–25), and they have been shown to have estrogenic effects in cell models and experimental animals (26). Although the role of phthalates in humans is less clear

(26), cross-sectional data from the Third National Health and Nutrition Examination Survey (NHANES) show that self-reported history of uterine leiomyomata was positively associated with urinary levels of monobutyl phthalate and inversely associated with urinary levels of mono(2-ethylhexyl) phthalate (27). In contrast, a case-control study found significantly higher levels of total urinary monoethylhexyl phthalate in uterine leiomyomata cases than controls (28). Additional studies investigating the association of putative endocrine-disrupting chemicals (e.g., diethylstilbestrol, polychlorinated biphenyls, and dioxin) with uterine leiomyomata risk have also found positive associations (29–31), but others have shown inverse (32) and null (33–35) associations.

In this hypothesis-generating study, we prospectively evaluated the association between hair relaxer use and uterine leiomyomata risk in a large population of premenopausal black women. We also explored whether the percentage of European ancestry (measured by a panel of European and African ancestry informative polymorphisms), which we hypothesized would be associated with both hair relaxer use and uterine leiomyomata, was a potential confounder of the relation. To our knowledge, there are no previous studies of the relation between chemical hair relaxers and risk of uterine leiomyomata.

## MATERIALS AND METHODS

### Study population

The Black Women's Health Study is an ongoing US prospective cohort study of 59,000 African-American women aged 21–69 years at entry (36). In 1995, *Essence* magazine subscribers, black members of 2 professional societies, and friends and relatives of early respondents were mailed an invitation to enroll in a long-term health study by completing a comprehensive self-administered baseline questionnaire. Every 2 years, participants are asked to update exposure and medical histories by questionnaire. Study participants reside in more than 17 states, with the majority residing in New York, California, Illinois, Michigan, Georgia, and New Jersey. The Institutional Review Board of Boston University Medical Center approved the study protocol.

### Assessment of outcome

On the 1999 and 2001 follow-up questionnaires, women reported whether they had been diagnosed with “uterine fibroids” in the previous 2-year interval, the calendar year in which they were first diagnosed, and whether their diagnosis was confirmed by “pelvic exam” and/or by “ultrasound/hysterectomy.” On the 2003, 2005, 2007, and 2009 follow-up questionnaires, “hysterectomy” was replaced by “surgery (e.g., hysterectomy)” to capture women who had other surgeries such as myomectomy, and “ultrasound” and “surgery” were divided into separate questions. Cases were classified as “surgically-confirmed” if they reported diagnosis by “surgery” on the 2003 or later questionnaires, or if they reported a diagnosis by “ultrasound/hysterectomy” and also reported “hysterectomy” under a separate question in 1999 or 2001.

We included cases diagnosed by ultrasound as well as surgery because the latter represent only 10%–30% of diagnosed cases and because studies of such cases may spuriously identify risk factors associated with severity or treatment preference (37). Ultrasound has high sensitivity (99%) and specificity (91%) relative to histologic evidence (38, 39). To maximize the specificity of uterine leiomyomata classification, pelvic examination cases ( $n = 538$ ) were treated as noncases because these diagnoses could have represented other gynecologic pathology (40).

### Assessment of hair relaxer use and covariates

The baseline 1995 questionnaire collected data on several risk factors for uterine leiomyomata, including reproductive and contraceptive history; anthropometric factors; lifestyle factors (smoking, alcohol, physical activity); geographic region of residence; socioeconomic correlates (education, marital status, occupation); medical history; and gynecologic surveillance (recency of cervical smear and pelvic examination). In 1997, women reported their country of birth. Biennial follow-up questionnaires updated information on risk factors and identified new cases of uterine leiomyomata. Reproductive factors, weight, smoking, marital status, physical activity, and region were updated on follow-up questionnaires and were modeled as time-varying covariates in the analyses.

During 2002–2007, 50% of study participants provided a mouthwash-saliva sample as a source of DNA (41). As part of a genetic admixture mapping study in our cohort (42–44), we used a set of ancestral informative genetic polymorphisms to estimate percentage of European ancestry for 2,259 uterine leiomyomata cases and 2,154 unaffected women who had provided a DNA sample. Average “European ancestry” among African Americans is estimated to be 20% (45).

The 1997 follow-up questionnaire included questions about use of “chemical hair straighteners”: age at first use (<10, 10–19, 20–29,  $\geq 30$  years); frequency of use per year (about 1 time, 2 times, 3–4 times, 5–6 times,  $\geq 7$  times); total number of years of use (<1, 1–4, 5–9, 10–14, 15–19,  $\geq 20$ ); number of burns (a break in the skin, not just tingling) during the application of chemical straighteners (never, 1–2, 3–4, 5–9,  $\geq 10$  times); and type of formulation used most often (lye, no-lye, don't know).

### Validation studies

With regard to uterine leiomyomata, a random sample of cases ( $n = 248$ ) were mailed supplemental questionnaires regarding their initial date of diagnosis, method(s) of confirmation, symptoms, and treatment, and they were asked for permission to review their medical records. We obtained medical records from 127 of the 128 women who gave us permission and confirmed the self-report in 122 (96%). Among the 188 (76%) who provided supplemental survey data, 71% reported uterine leiomyomata-related symptoms prior to diagnosis, and 87% reported that their condition came to clinical attention because they sought treatment for symptoms or a tumor was palpable during a routine pelvic examination. There were no appreciable differences

between cases who did and did not release medical records with respect to uterine leiomyomata risk factors (46).

### Restriction criteria

Follow-up began in 1997 because the method of uterine leiomyomata diagnosis was first included on the 1999 questionnaire. Of the 53,126 respondents to the 1997 questionnaire, we excluded postmenopausal women ( $n = 16,478$ ) in whom uterine leiomyomata are rare (47); women with a history of uterine leiomyomata ( $n = 10,655$ ); women who did not complete a questionnaire after 1997 ( $n = 940$ ); cases without data on diagnosis year ( $n = 120$ ) or method ( $n = 112$ ); and women with missing exposure ( $n = 659$ ) or covariate data ( $n = 582$ ), leaving 23,580 women for analysis. Those excluded had lower educational attainment than those included but were similar with respect to parity, age at menarche, and other established uterine leiomyomata risk factors.

### Data analysis

We defined cases as women who reported a first diagnosis of uterine leiomyomata confirmed by ultrasound or surgery. Person-years were calculated from March 1997 until uterine leiomyomata diagnosis ( $n = 7,146$ ), menopause ( $n = 2,639$ ), death ( $n = 372$ ), loss to follow-up ( $n = 3,393$ ), or March 2009 ( $n = 10,030$ ), whichever came first. Age- and period-stratified Cox regression was used to estimate incidence rate ratios and 95% confidence intervals for the associations of interest.

Hair relaxer variables were categorized according to their frequency distributions in the analytical sample. We also created a hair relaxer score variable, the product of frequency and duration of use, after first converting them to continuous variables by assigning values to the midpoint of each category. We defined “never users” as those who reported never using hair relaxers or having used them for less than 1 year in total. A covariate was included in multivariable analyses if it was either an established risk factor for uterine leiomyomata identified from the literature or a potential risk factor for uterine leiomyomata associated with hair relaxer use. On the basis of these criteria, we constructed a multivariable model that controlled for age (1-year intervals), time period (2-year intervals), age at menarche (years), parity (births), age at first birth (years), years since last birth (<5, 5–9, 10–14, 15,  $\geq 20$ ), oral contraceptive use (never, current, past), body mass index (<20, 20–24, 25–29, 30–34,  $\geq 35$  kg/m<sup>2</sup>), smoking (current, past, never), current alcohol use (<1, 1–6,  $\geq 7$  drinks/week), education ( $\leq 12$ , 13–15, 16,  $\geq 17$  years), marital status (married/partnered, divorced/separated/widowed, single), occupation (white collar, non-white collar, unemployed, missing), household income ( $\leq \$25,000$ , \$25,001–\$50,000, \$50,001–\$100,000,  $> \$100,000$ , missing), geographic region (South, Northeast, Midwest, and West), and country of birth (United States vs. outside United States).

Tests for trend were conducted by modeling the ordinal categorical version of the exposure variable among the ever users of hair relaxers (48). We used stratification methods to

examine whether main associations were modified by other covariates such as body mass index, education, and geographic region. *P* values from interaction tests were obtained by using the likelihood ratio test comparing models with and without cross-product terms between the covariate and exposure variable. Departures from proportional hazards were evaluated in the same manner by using cross-product terms between each exposure variable and age (<35 vs.  $\geq 35$  years) and time period (1997–2003 vs. 2003–2009). Analyses were performed by using SAS, version 9.2, statistical software (49).

### RESULTS

Nearly 94% of women in our cohort reported using hair relaxers for at least 1 year (Table 1). The frequency of hair relaxer use ranged from as low as 8.6% for 1–2 times per year to as high as 32.6% for  $\geq 7$  times per year. Frequency of use was highest among participants who were current users of oral contraceptives, had higher income, had a white collar occupation, had higher educational attainment, resided in the South or Midwest, or were foreign born; it was lowest among older women and women who resided in the West or Northeast. Among the 2,259 cases and 2,154 non-cases for whom we had genotyping data, the frequency of hair relaxer use increased with decreasing percentage of European ancestry. Weak correlations were observed between frequency and duration (Spearman's correlation coefficient ( $r$ ) = 0.22,  $P < 0.001$ ), frequency and number of burns ( $r$  = 0.23,  $P < 0.001$ ), and duration and number of burns ( $r$  = 0.17,  $P < 0.001$ ) (data not shown).

During 199,991 person-years of observation, 7,146 incident cases of uterine leiomyomata diagnosed by ultrasound ( $n = 4,630$ ) or surgery ( $n = 2,516$ ) were reported (Table 2). The multivariable incidence rate ratio for hair relaxer use relative to nonuse was 1.17 (95% confidence interval (CI): 1.06, 1.30). There was no clear pattern of risk for age at first use of hair relaxers. Multivariable incidence rate ratios increased monotonically with increasing frequency of use ( $P_{\text{trend}} < 0.001$ ), and the incidence rate ratio comparing frequency of use  $\geq 7$  times per year versus never use was 1.23 (95% CI: 1.10, 1.37). Duration of use and number of burns were also positively associated with risk of uterine leiomyomata, but there was no clear dose-response relation. There was no association with type of formulation used most often (lye vs. no-lye), although nearly 10% of women reported “don't know” to this question. The score variable, which incorporated data on frequency and duration of hair relaxer use, showed evidence of a dose-response relation. Relative to quintile 1, the multivariable incidence rate ratio increased from 1.09 (95% CI: 0.97, 1.22) for quintile 2 to 1.25 (95% CI: 1.12, 1.40) for quintile 5 ( $P_{\text{trend}} < 0.001$ ).

Among the long-term hair relaxer users (i.e.,  $\geq 10$  years of use), positive trends for frequency of use were found overall (Table 3). None of the incidence rate ratios differed statistically across strata of body mass index, education, or region (Table 3), but associations appeared to be stronger among leaner women and women living in the South. Notably, there was virtually no association observed among obese women (body mass index  $\geq 30$ ). Results were also similar across

**Table 1.** Characteristics of 23,580 Women According to Hair Relaxer Use, The Black Women's Health Study, United States, 1997<sup>a</sup>

|  | Never Use<br>(n = 1,491) <sup>b</sup> |      | Frequency of Use per Year |      |      |      |      |      |
|--|---------------------------------------|------|---------------------------|------|------|------|------|------|
|  | %                                     | Mean | %                         | Mean | %    | Mean | %    | Mean |
| Age, years                                   |                                       | 36.5 |                           | 36.0 |      | 35.7 |      | 34.6 |
| Body mass index <sup>c</sup>                 |                                       | 27.3 |                           | 27.8 |      | 28.4 |      | 27.8 |
| Age at menarche, years                       |                                       | 12.5 |                           | 12.3 |      | 12.3 |      | 12.3 |
| Pelvic examination in 2007                   | 83.4                                  |      | 87.3                      |      | 88.5 |      | 90.6 |      |
| Parous                                       | 54.9                                  |      | 59.6                      |      | 60.6 |      | 56.4 |      |
| Age at first birth (parous), years           |                                       | 22.9 |                           | 23.0 |      | 23.0 |      | 23.3 |
| Current use of oral contraceptives           | 21.4                                  |      | 21.5                      |      | 21.7 |      | 23.8 |      |
| Current smoker                               | 13.9                                  |      | 17.2                      |      | 15.2 |      | 13.5 |      |
| Alcoholic drinks per week                    |                                       | 1.2  |                           | 1.3  |      | 1.3  |      | 1.3  |
| Married                                      | 36.7                                  |      | 38.2                      |      | 40.7 |      | 39.8 |      |
| Education in 1995, years                     |                                       | 14.7 |                           | 14.6 |      | 14.7 |      | 15.0 |
| White collar occupation in 1995              | 49.4                                  |      | 51.2                      |      | 52.3 |      | 55.5 |      |
| Household income in 2003                     |                                       |      |                           |      |      |      |      |      |
| ≤\$25,000                                    | 13.3                                  |      | 11.3                      |      | 10.0 |      | 7.5  |      |
| \$25,001–\$50,000                            | 26.0                                  |      | 25.4                      |      | 26.0 |      | 24.4 |      |
| \$50,001–\$100,000                           | 25.2                                  |      | 28.6                      |      | 30.8 |      | 33.3 |      |
| >\$100,000                                   | 13.5                                  |      | 12.2                      |      | 13.0 |      | 15.4 |      |
| Region of residence in the United States     |                                       |      |                           |      |      |      |      |      |
| Northeast                                    | 28.1                                  |      | 31.1                      |      | 30.7 |      | 27.5 |      |
| Midwest                                      | 18.1                                  |      | 20.6                      |      | 21.3 |      | 22.7 |      |
| West   | 30.6                                  |      | 22.8                      |      | 18.6 |      | 17.0 |      |
| South  | 23.3                                  |      | 25.5                      |      | 29.2 |      | 32.7 |      |
| Foreign born                                 | 6.4                                   |      | 6.1                       |      | 6.5  |      | 6.2  |      |
| Percentage of European ancestry <sup>d</sup> |                                       | 27.8 |                           | 27.5 |      | 21.6 |      | 20.1 |

<sup>a</sup> Values are standardized to the age distribution of the study population.<sup>b</sup> Never users include those who used hair relaxers for less than 1 year.<sup>c</sup> Body mass index: weight (kg)/height (m)<sup>2</sup>.<sup>d</sup> Restricted to 4,413 women with genotyping data.

age (Table 3) and different time periods of study observation (data not shown), indicating that the proportional hazards assumption was met. Results for ever use and duration of use of hair relaxers were somewhat stronger among surgical cases, but results for frequency of use did not differ according to method of diagnosis (data not shown). Finally, when the sample was confined to the 7,741 women who reported a pelvic ultrasound examination within 5 years of the 2007 questionnaire (4,134 cases and 61,948 person-years), a subgroup of women for whom undiagnosed uterine leiomyomata are less likely, results were slightly stronger than those found in the whole sample: Multivariable incidence rate ratios comparing frequency of use 3–4, 5–6, and ≥7 times/year with 1–2 times/year were 1.18 (95% CI: 0.99, 1.42), 1.19 (95% CI: 0.99, 1.41), and 1.25 (95% CI: 1.05, 1.49) ( $P_{\text{trend}} = 0.02$ ).

Table 4 presents results for selected hair relaxer variables in relation to uterine leiomyomata risk among women for whom genotyping data were available ( $n = 4,413$ ). Weakly

positive findings were still found for ever use, frequency of use, duration of use, number of burns, and hair relaxer score. Effect estimates were attenuated when we controlled for percentage of European ancestry.

## DISCUSSION

In this large population of premenopausal US black women, we observed increased risks of uterine leiomyomata in association with ever use of hair relaxers, duration of use, frequency of use, and total number of burns experienced during use. A composite variable for frequency and duration of use showed evidence of a dose-response relation. Positive associations were also observed between frequency of hair relaxer use and risk of uterine leiomyomata among the long-term users (i.e., duration of use ≥ 10 years). We found no association of uterine leiomyomata with age at first use or type of formulation used. Although stronger associations

**Table 2.** Hair Relaxer Use and Risk of Uterine Leiomyomata, The Black Women's Health Study, United States, 1997–2009

|   | Cases,<br>no. | Person-<br>Years, no. | IRR <sup>a</sup> | 95% CI     | IRR <sup>b</sup> | 95% CI     |
|---|---------------|-----------------------|------------------|------------|------------------|------------|
| Hair relaxer use                            |               |                       |                  |            |                  |            |
| Never use or <1 year of use                 | 380           | 12,766                | 1.00             | Referent   | 1.00             | Referent   |
| Ever  | 6,766         | 187,225               | 1.22             | 1.10, 1.36 | 1.17             | 1.06, 1.30 |
| Age at first use, years                     |               |                       |                  |            |                  |            |
| <10   | 512           | 15,122                | 1.20             | 1.05, 1.38 | 1.14             | 0.99, 1.30 |
| 10–19                                       | 4,833         | 131,766               | 1.25             | 1.13, 1.39 | 1.20             | 1.08, 1.33 |
| ≥20   | 1,421         | 40,337                | 1.15             | 1.03, 1.29 | 1.12             | 0.99, 1.25 |
| <i>P</i> <sub>trend</sub> among exposed     |               |                       |                  | 0.09       |                  | 0.27       |
| Frequency of use, times/year                |               |                       |                  |            |                  |            |
| 1–2   | 540           | 17,152                | 1.06             | 0.93, 1.21 | 1.06             | 0.93, 1.21 |
| 3–4   | 1,650         | 48,646                | 1.14             | 1.02, 1.28 | 1.11             | 0.99, 1.25 |
| 5–6   | 2,102         | 55,949                | 1.27             | 1.14, 1.41 | 1.20             | 1.08, 1.34 |
| ≥7  | 2,474         | 65,478                | 1.30             | 1.16, 1.44 | 1.23             | 1.10, 1.37 |
| <i>P</i> <sub>trend</sub> among exposed     |               |                       |                  | <0.001     |                  | <0.001     |
| Duration of use, years                      |               |                       |                  |            |                  |            |
| 1–4   | 379           | 12,585                | 1.03             | 0.89, 1.19 | 1.03             | 0.89, 1.19 |
| 5–9   | 783           | 23,415                | 1.20             | 1.06, 1.36 | 1.17             | 1.04, 1.33 |
| 10–14                                       | 1,814         | 53,502                | 1.20             | 1.07, 1.35 | 1.15             | 1.03, 1.29 |
| 15–19                                       | 2,074         | 53,296                | 1.27             | 1.14, 1.42 | 1.21             | 1.08, 1.35 |
| ≥20   | 1,716         | 44,427                | 1.26             | 1.12, 1.40 | 1.20             | 1.07, 1.34 |
| <i>P</i> <sub>trend</sub> among exposed     |               |                       |                  | <0.001     |                  | 0.015      |
| No. of burns                                |               |                       |                  |            |                  |            |
| Never burned                                | 851           | 25,891                | 1.11             | 0.99, 1.26 | 1.08             | 0.96, 1.22 |
| 1–2 times                                   | 1,815         | 51,384                | 1.19             | 1.06, 1.33 | 1.14             | 1.02, 1.28 |
| 3–4 times                                   | 1,494         | 41,419                | 1.23             | 1.10, 1.37 | 1.17             | 1.04, 1.31 |
| 5–9 times                                   | 1,060         | 27,956                | 1.29             | 1.15, 1.45 | 1.25             | 1.11, 1.40 |
| ≥10 times                                   | 1,546         | 40,576                | 1.30             | 1.16, 1.46 | 1.23             | 1.10, 1.38 |
| <i>P</i> <sub>trend</sub> among exposed     |               |                       |                  | <0.001     |                  | <0.001     |
| Formulation used most often                 |               |                       |                  |            |                  |            |
| No lye                                      | 4,886         | 136,114               | 1.22             | 1.10, 1.35 | 1.18             | 1.06, 1.31 |
| Lye   | 1,225         | 31,935                | 1.29             | 1.15, 1.44 | 1.21             | 1.08, 1.36 |
| Don't know                                  | 655           | 19,176                | 1.17             | 1.03, 1.32 | 1.09             | 0.96, 1.24 |
| Hair relaxer score (quintiles) <sup>c</sup> |               |                       |                  |            |                  |            |
| <43   | 1,162         | 27,330                | 1.10             | 0.98, 1.23 | 1.09             | 0.97, 1.22 |
| 43–67                                       | 1,202         | 25,890                | 1.19             | 1.06, 1.34 | 1.16             | 1.03, 1.30 |
| 68–92                                       | 933           | 44,165                | 1.22             | 1.08, 1.37 | 1.16             | 1.03, 1.31 |
| 93–135                                      | 1,865         | 50,273                | 1.26             | 1.13, 1.40 | 1.20             | 1.07, 1.34 |
| ≥136  | 1,604         | 39,568                | 1.33             | 1.19, 1.48 | 1.25             | 1.12, 1.40 |
| <i>P</i> <sub>trend</sub> among exposed     |               |                       |                  | <0.001     |                  | <0.001     |

Abbreviations: CI, confidence interval; IRR, incidence rate ratio.

<sup>a</sup> Adjusts for age and time period.<sup>b</sup> Adjusts for age, time period, parity, age at first birth, years since last birth, ever use of oral contraceptive and age at first use, body mass index, smoking status, current alcohol intake, education, income, occupation, marital status, country of birth, and region of residence in the United States.<sup>c</sup> Hair relaxer score = frequency (no. of times/year) × duration (no. of years).

**Table 3.** Hair Relaxer Use and Risk of Uterine Leiomyomata Among Women With  $\geq 10$  Years of Hair Relaxer Use, The Black Women's Health Study, United States, 1997–2009

|                              | Frequency of Hair Relaxer Use (Times per Year) |                   |                  |          |            |                   |                  |            |            |                   |                  |            |            |                   |                  |            | <i>P</i> <sub>trend</sub> | <i>P</i> <sub>Interaction</sub> |
|------------------------------|--|-------------------|------------------|----------|------------|-------------------|------------------|------------|------------|-------------------|------------------|------------|------------|-------------------|------------------|------------|---------------------------|---------------------------------|
|                              | 1–2  |                   |                  |          | 3–4        |                   |                  |            | 5–6        |                   |                  |            | ≥7         |                   |                  |            |                           |                                 |
|                              | Cases, no.                                     | Person-Years, no. | IRR <sup>a</sup> | 95% CI   | Cases, no. | Person-Years, no. | IRR <sup>a</sup> | 95% CI     | Cases, no. | Person-Years, no. | IRR <sup>a</sup> | 95% CI     | Cases, no. | Person-Years, no. | IRR <sup>a</sup> | 95% CI     |                           |                                 |
| All women                    | 274  | 8,355             | 1.00             | Referent | 1,280      | 36,921            | 1.04             | 0.92, 1.19 | 1,812      | 47,541            | 1.12             | 0.99, 1.27 | 2,238      | 58,408            | 1.15             | 1.01, 1.31 | 0.002                     |                                 |
| Age, years                   |  |                   |                  |          |            |                   |                  |            |            |                   |                  |            |            |                   |                  |            |                           | 0.95                            |
| <35                          | 59   | 2,158             | 1.00             | Referent | 313        | 10,426            | 1.08             | 0.82, 1.43 | 515        | 15,699            | 1.14             | 0.89, 1.49 | 773        | 22,949            | 1.22             | 0.93, 1.59 | 0.03                      |                                 |
| ≥35                          | 215  | 6,197             | 1.00             | Referent | 967        | 26,495            | 1.03             | 0.89, 1.20 | 1,297      | 31,841            | 1.12             | 0.97, 1.29 | 1,465      | 35,459            | 1.13             | 0.98, 1.31 | 0.02                      |                                 |
| Body mass index <sup>b</sup> |  |                   |                  |          |            |                   |                  |            |            |                   |                  |            |            |                   |                  |            |                           | 0.10                            |
| <25                          | 79   | 2,725             | 1.00             | Referent | 352        | 11,242            | 1.05             | 0.82, 1.34 | 636        | 16,012            | 1.30             | 1.02, 1.64 | 731        | 19,479            | 1.26             | 1.00, 1.59 | 0.003                     |                                 |
| 25–29                        | 79   | 2,446             | 1.00             | Referent | 399        | 10,772            | 1.17             | 0.92, 1.49 | 554        | 14,356            | 1.19             | 0.94, 1.51 | 724        | 18,564            | 1.22             | 0.97, 1.54 | 0.15                      |                                 |
| ≥30                          | 116  | 3,185             | 1.00             | Referent | 529        | 14,907            | 0.96             | 0.78, 1.17 | 622        | 17,172            | 0.95             | 0.78, 1.16 | 783        | 20,365            | 1.04             | 0.86, 1.27 | 0.23                      |                                 |
| Education, years             |  |                   |                  |          |            |                   |                  |            |            |                   |                  |            |            |                   |                  |            |                           | 0.07                            |
| <16                          | 152  | 4,886             | 1.00             | Referent | 702        | 19,978            | 1.14             | 0.96, 1.36 | 871        | 23,113            | 1.20             | 1.01, 1.43 | 1,054      | 29,150            | 1.19             | 1.00, 1.41 | 0.11                      |                                 |
| ≥16                          | 122  | 3,469             | 1.00             | Referent | 578        | 16,943            | 0.93             | 0.76, 1.13 | 941        | 24,428            | 1.03             | 0.85, 1.25 | 1,184      | 29,258            | 1.10             | 0.91, 1.33 | 0.003                     |                                 |
| Geographic region            |  |                   |                  |          |            |                   |                  |            |            |                   |                  |            |            |                   |                  |            |                           | 0.42                            |
| Northeast                    | 83   | 2,632             | 1.00             | Referent | 379        | 10,794            | 1.08             | 0.85, 1.38 | 489        | 13,205            | 1.12             | 0.89, 1.42 | 522        | 13,323            | 1.18             | 0.93, 1.49 | 0.09                      |                                 |
| Midwest                      | 72   | 1,645             | 1.00             | Referent | 272        | 8,395             | 0.75             | 0.57, 0.97 | 410        | 10,842            | 0.87             | 0.67, 1.12 | 515        | 13,829            | 0.89             | 0.69, 1.14 | 0.26                      |                                 |
| West                         | 50   | 1,683             | 1.00             | Referent | 208        | 6,246             | 1.11             | 0.81, 1.52 | 291        | 7,533             | 1.26             | 0.93, 1.71 | 273        | 8,207             | 1.09             | 0.80, 1.48 | 0.85                      |                                 |
| South                        | 69   | 2,383             | 1.00             | Referent | 419        | 11,448            | 1.24             | 0.96, 1.60 | 621        | 15,911            | 1.28             | 1.00, 1.64 | 922        | 22,985            | 1.38             | 1.08, 1.77 | 0.004                     |                                 |

Abbreviations: CI, confidence interval; IRR, incidence rate ratio.

<sup>a</sup> Adjusts for age, time period, parity, age at first birth, years since last birth, ever use of oral contraceptive and age at first use, body mass index, smoking status, current alcohol intake, education, income, occupation, marital status, country of birth, and region of residence in the United States, when applicable.<sup>b</sup> Body mass index: weight (kg)/height (m)<sup>2</sup>.

**Table 4.** Hair Relaxer Use and Risk of Uterine Leiomyomata in a Subset of 2,259 Cases and 2,154 Noncases With Genotyping Data, The Black Women's Health Study, United States, 1997–2009

|   | Cases,<br>no. | Person-<br>Years, no. | IRR <sup>a</sup> | 95% CI     | IRR <sup>b</sup> | 95% CI     | IRR <sup>c</sup> | 95% CI     |
|---|---------------|-----------------------|------------------|------------|------------------|------------|------------------|------------|
| Hair relaxer use                            |               |                       |                  |            |                  |            |                  |            |
| Never use or <1 year of use                 | 109           | 2,161                 | 1.00             | Referent   | 1.00             | Referent   | 1.00             | Referent   |
| Ever  | 2,150         | 33,518                | 1.33             | 1.10, 1.62 | 1.26             | 1.04, 1.53 | 1.19             | 0.97, 1.44 |
| Frequency of use, times/year                |               |                       |                  |            |                  |            |                  |            |
| 1–2   | 154           | 2,941                 | 1.06             | 0.83, 1.35 | 1.04             | 0.82, 1.34 | 1.05             | 0.82, 1.34 |
| 3–4   | 473           | 7,809                 | 1.25             | 1.01, 1.54 | 1.20             | 0.97, 1.48 | 1.14             | 0.92, 1.41 |
| 5–6   | 711           | 9,923                 | 1.48             | 1.21, 1.81 | 1.37             | 1.12, 1.68 | 1.30             | 1.05, 1.59 |
| ≥7  | 812           | 12,846                | 1.35             | 1.11, 1.65 | 1.27             | 1.03, 1.55 | 1.18             | 0.96, 1.45 |
| $P_{\text{trend}}$ among exposed            |               |                       |                  | 0.007      |                  | 0.06       |                  | 0.30       |
| Duration of use, years                      |               |                       |                  |            |                  |            |                  |            |
| 1–4   | 114           | 2,253                 | 1.03             | 0.79, 1.34 | 1.03             | 0.79, 1.34 | 0.99             | 0.76, 1.29 |
| 5–9   | 254           | 4,205                 | 1.37             | 1.09, 1.72 | 1.33             | 1.06, 1.67 | 1.26             | 1.00, 1.59 |
| 10–14                                       | 584           | 9,756                 | 1.35             | 1.10, 1.66 | 1.26             | 1.02, 1.56 | 1.18             | 0.96, 1.46 |
| 15–19                                       | 662           | 9,662                 | 1.40             | 1.14, 1.71 | 1.29             | 1.05, 1.59 | 1.22             | 0.99, 1.50 |
| ≥20   | 536           | 7,642                 | 1.32             | 1.07, 1.63 | 1.26             | 1.02, 1.56 | 1.19             | 0.96, 1.47 |
| $P_{\text{trend}}$ among exposed            |               |                       |                  | 0.11       |                  | 0.29       |                  | 0.36       |
| No. of burns                                |               |                       |                  |            |                  |            |                  |            |
| Never burned                                | 252           | 4,161                 | 1.22             | 0.98, 1.53 | 1.14             | 0.91, 1.43 | 1.09             | 0.87, 1.37 |
| 1–2 times                                   | 551           | 8,864                 | 1.29             | 1.05, 1.58 | 1.22             | 0.99, 1.51 | 1.16             | 0.94, 1.43 |
| 3–4 times                                   | 498           | 7,723                 | 1.33             | 1.08, 1.64 | 1.26             | 1.02, 1.56 | 1.18             | 0.95, 1.46 |
| 5–9 times                                   | 353           | 5,075                 | 1.48             | 1.19, 1.83 | 1.40             | 1.13, 1.75 | 1.32             | 1.06, 1.64 |
| ≥10 times                                   | 496           | 7,694                 | 1.37             | 1.11, 1.69 | 1.28             | 1.03, 1.58 | 1.20             | 0.97, 1.49 |
| $P_{\text{trend}}$ among exposed            |               |                       |                  | 0.06       |                  | 0.07       |                  | 0.11       |
| Hair relaxer score (quintiles) <sup>d</sup> |               |                       |                  |            |                  |            |                  |            |
| <43   | 362           | 6,305                 | 1.21             | 0.97, 1.50 | 1.18             | 0.95, 1.47 | 1.15             | 0.92, 1.42 |
| 43–67                                       | 351           | 6,023                 | 1.25             | 1.01, 1.55 | 1.19             | 0.96, 1.48 | 1.13             | 0.90, 1.40 |
| 68–92                                       | 283           | 4,175                 | 1.40             | 1.12, 1.75 | 1.30             | 1.04, 1.63 | 1.23             | 0.98, 1.54 |
| 93–135                                      | 641           | 9,544                 | 1.42             | 1.16, 1.74 | 1.32             | 1.07, 1.62 | 1.24             | 1.00, 1.52 |
| ≥136  | 513           | 7,472                 | 1.37             | 1.11, 1.69 | 1.28             | 1.04, 1.58 | 1.19             | 0.96, 1.47 |
| $P_{\text{trend}}$ among exposed            |               |                       |                  | 0.003      |                  | 0.22       |                  | 0.54       |

Abbreviations: CI, confidence interval; IRR, incidence rate ratio.

<sup>a</sup> Adjusts for age and time period.<sup>b</sup> Adjusts for age, time period, parity, age at first birth, years since last birth, ever use of oral contraceptive and age at first use, body mass index, smoking status, current alcohol intake, education, income, occupation, marital status, country of birth, and region of residence in the United States.<sup>c</sup> Adjusts for percentage of European ancestry in addition to all the variables listed in footnote b.<sup>d</sup> Hair relaxer score = frequency (no. of times/year) × duration (no. of years).

were seen for leaner women and women living in the South, there was no evidence of statistical interaction by body mass index or region. The stronger results for surgically confirmed uterine leiomyomata cases may be explained by the higher rates of uterine leiomyomata-related hysterectomy in the South (50, 51), the region in which the prevalence of hair relaxer use was greatest. Adjustment for genetic admixture (i.e., percentage of European ancestry) among the subset of women with genotyping data showed appreciable attenuation of effect estimates, but genetic admixture did not fully explain the positive associations.

Systematic bias in the reporting of hair relaxer use by case status is unlikely because reports of hair relaxer use were ascertained prior to the diagnosis of uterine leiomyomata. Any random misclassification of hair relaxer use would have diluted associations for the extreme categories of exposure. Although we assessed history of hair relaxer use at a single point in time only (i.e., in 1997), results were similar across the different time periods of study observation. Retention of the baseline cohort was approximately 80% through 2009, thereby minimizing potential for bias due to differential loss to follow-up. Our validation study of uterine leiomyomata

indicated high accuracy in reporting, and we controlled for a wide range of potential confounders. Moreover, stronger results were observed in subgroups of women among whom misclassification of uterine leiomyomata is lower (e.g., younger women and women with a recent pelvic ultrasound examination) (4). The large sample size and high incidence of uterine leiomyomata in this population conferred excellent statistical power to detect small increases in risk.

Because lye relaxers are thought to contain harsher chemicals (e.g., sodium hydroxide) than no-lye formulations, we hypothesized that women who more often used lye relaxers would have a higher risk of scalp lesions or burns, thereby increasing dermal absorption of putative endocrine-disrupting chemicals. One potential explanation for the lack of difference in association between lye and no-lye formulations is that both products pose a similar likelihood of scalp lesions and burns. Scalp inflammation and scarring alopecia have been documented anecdotally with both lye and no-lye relaxers (16). In addition, although most women currently reported using no-lye formulations, most had probably used lye formulations in the past (16), which could have diluted the association.

The study had no information on the individual brands of chemical relaxers used or on constituents that might be considered estrogen disruptors. Thus, we are unable to provide insight as to the specific mechanisms by which hair relaxers could have influenced risk. It is possible that hair relaxer use is a proxy for exposure to other products containing high levels of endocrine-disrupting chemicals (17) and that the hair relaxers themselves are not the causal agents. For instance, it has been documented that US black women have higher mean levels of exposure to environmental chemicals such as phthalates (52), bisphenol A (53), and common insecticides (54) than other ethnic groups. Finally, we observed that the percentage of European ancestry decreased with increasing use of hair relaxers in a subset of women from our cohort, and that adjustment for genetic admixture attenuated the observed associations for hair relaxer use and uterine leiomyomata incidence. Therefore, although our study raises the hypothesis that hair relaxer use is associated with an increased risk of uterine leiomyomata, we cannot rule out the possibility that greater African ancestry, thought to increase genetic predisposition to uterine leiomyomata (55), explains part or all of the observed association. Future studies are needed to confirm whether hair relaxer use and uterine leiomyomata are indeed associated.

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