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Associations of hair dye and relaxer use with breast tumor clinicopathologic features: findings from the Women's Circle of Health Study

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Declaration of interests

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

DATA SHARING

The data supporting the findings of this study are available upon reasonable request from the corresponding author. The data are not publicly available due to privacy or ethical restrictions. Information on requesting data can be found at: https://www.cinj.org/research/about-womens-circle-health-study.

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Abstract

BACKGROUND: Building upon our earlier findings of significant associations between hair dye and relaxer use with increased breast cancer risk, we evaluated associations of select characteristics of use with breast tumor clinicopathology.

METHODS: Using multivariable-adjusted models we examined the associations of interest in a case-only study of 2,998 women with breast cancer, overall and stratified by race and estrogen receptor (ER) status, addressing multiple comparisons using Bonferroni correction.

RESULTS: Compared to salon application of permanent hair dye, home kit and combination application (both salon and home kit application) were associated with increased odds of poorly differentiated tumors in the overall sample. This association was consistent among Black (home kit: OR 2.22, 95% CI: 1.21–5.00; combination: OR 2.46, 95% CI: 1.21–5.00), but not White women, and among ER+ (home kit: OR 1.47, 95% CI: 0.82–2.63; combination: OR 2.98, 95% CI: 1.62–5.49) but not ER− cases. Combination application of relaxers was associated with increased odds of tumors >2.0 cm vs. <1.0 cm (OR = 1.82, 95% CI: 1.23–2.69). Longer duration and earlier use of relaxers and combination application of permanent hair dyes and relaxers were associated with breast tumor features including higher tumor grade and larger tumor size, which often denote more aggressive phenotypes, although the findings did not maintain significance with Bonferroni correction.

CONCLUSIONS: These novel data support reported associations between hair dye and relaxer use with breast cancer, showing for the first time, associations with breast tumor clinicopathologic features. Improved hair product exposure measurement is essential for fully understanding the impact of these environmental exposure with breast cancer and to guide risk reduction strategies in the future.

Keywords

breast cancer; personal care products; hair products; hair dye; hair relaxer; breast tumor features

INTRODUCTION

Breast cancer is the most frequently diagnosed cancer among women in the United States, and accounts for the second highest cancer mortality rate (after lung cancer) (1). Clinically, Black women tend to be diagnosed with more aggressive breast cancers (e.g., characterized as poorly differentiated and hormone receptor-negative [HR−], with a greater propensity for positive lymph node status and metastasis) compared to White women (1, 2). Further, the triple-negative (TN) subtype—associated with the worst prognosis—has the highest incidence among Black women compared to women of other races/ethnicities (2). Of interest, use of hair dyes and relaxers is a suspected risk factor for breast cancer (3–26), though a causal relationship between this exposure and breast cancer risk has not been established. Most recently, it has been hypothesized to be associated with disparities in breast cancer phenotype (6, 13).

Hair products (and other personal care products) are environmental sources of exposure to endocrine-disrupting chemicals (EDCs) and mutagenic and/or genotoxic compounds, which are suspected contributors to breast carcinogenesis. Although the intended use of these products is topical, chemicals can gain systemic access through the skin. Data have shown greater use of EDC-containing hair products, including chemical relaxers (5, 13, 20, 27) and use of hair products that contain more harmful chemicals (28, 29) among Black women compared to their White counterparts. Furthermore, evidence supports that initiation of use of EDC-containing hair products occur at an earlier age among Black women and childhood use has been associated with earlier puberty (5, 27). Therefore, not only does early exposure to EDC-containing hair products increase cumulative lifetime exposure to potentially harmful compounds, but these products are also implicated as a contributor to earlier pubertal timing (30–32), which is in an important risk factor for breast cancer. In addition, while findings from several epidemiologic studies have historically suggested that hair dye use is associated with increased risk of hematopoietic neoplasms (14, 22, 33–35) and bladder cancer (24, 36–38), emerging data have suggested a positive association with breast cancer as well (6, 8, 13, 39). A meta-analysis examining the association between hair dye use and breast cancer risk in eight studies (N = 38,037) suggested a significant dose-dependent relationship (40). Recent findings from the Nurse's Health Study suggested that cumulative dose of permanent hair dye use was associated with increased risk of estrogen receptor negative (ER−), progesterone receptor negative (PR−), and HR− breast cancer, albeit in a cohort of predominantly non-Hispanic White (NHW) healthcare professionals (39). At present, however, a causal association between increased use of hair dyes and development of breast cancer cannot be confirmed.

In the current study, we sought to expand upon our earlier analysis in the Women's Circle of Health Study (WCHS), in which we observed significant associations between hair dye and relaxer use and breast cancer risk among Black and White women (13). In particular, here we examined whether certain characteristics of use of hair dyes and relaxers are associated with more aggressive tumor features, including larger tumor size, higher tumor grade, negative HR status, positive lymph node status, and tumor subtype – all of which play some role in prognostication, whether it is predicting survival outcome or recurrence risk, and have been associated with disease progression (41–43). Specifically, we hypothesized that greater duration and magnitude of exposure to hair dyes and relaxers, use of darker shades of hair dye and lye-based relaxers, as well as joint use of dyes and relaxers are associated with more aggressive tumor features. Given findings from our earlier analysis (13) and data from other studies (6, 39) suggesting potential differences in associations between hair product use and breast cancer by ER status, we hypothesized that the associations with tumor clinicopathologic features might also differ by ER status. With regards to application of hair dyes and relaxers, we hypothesized that home kit or combination of home kit and salon application, compared to salon application alone, are associated with more aggressive tumor features due to the possibility that self-application of these hair products (rather than having them applied by a professional in a salon setting) might equate to higher levels of exposure to potentially harmful chemicals. We examined the associations of interest with the hope of further understanding the role this particular environmental risk factor may play

in pathology, which might help inform strategies for breast cancer risk reduction among individuals who may be at increased risk and who regularly use these products.

MATERIALS AND METHODS

Study Participants

As previously described, the WCHS was a case–control study conducted in metropolitan New York City (NYC) and ten counties in New Jersey (NJ) (13). The current study included participants recruited from 2001 to 2018. Women with histologically confirmed ductal carcinoma *in situ* or invasive breast cancer (stages I–IV) who self-identified as either Black/African American or White/European American, were age 20–75 years, able to complete an interview in English, and had completed the baseline interview by the end of 2018 were eligible to participate. In 2014, recruitment of Black/African American cases in NJ continued with the establishment of the Women's Circle of Health Follow-up Study (WCHFS), a cohort of Black/African American breast cancer survivors in New Jersey (44). In the current case-only analysis, we included 2,998 breast cancer cases (2,227 Black and 771 White) who enrolled in the WCHS and WCHFS through 2018 and had complete baseline interview data available for analysis.

Data Collection

Data collection for the WCHS and WCHFS was conducted through in-person home visits approximately 9 months after diagnosis and included computer-assisted interviewing to administer questionnaires. Information on sociodemographic variables as well as established and probable breast cancer risk factors, including: family and personal health history, prenatal exposures, reproductive history, hormone use, and lifestyle factors (e.g., hair product use, tobacco smoke exposure, alcohol consumption, physical activity, dietary supplement use) were ascertained. Anthropometric measurements (height, weight, waist and hip circumferences and body composition measures) were also taken during the interview, using standardized protocols and instruments (45). Use of permanent hair dye and chemical relaxer/straightener were assessed in interviewer-administered questionnaires (13). Questions ascertained history of permanent hair dye use and patterns of use, non-inclusive of semi-permanent or temporary hair dye. Regular hair dye use was defined as 'having ever used permanent hair dye for at least 1 year at a rate of ≥2 times per year'. Regular chemical relaxer use (referred to as 'relaxer' hereafter) was defined as 'having ever chemically relaxed or straightened hair for at least 1 year'. Data on hair product use characteristics were also collected and included the following: total duration (years) of hair dye use (≤10 years, >10 years); typical shade of hair dye used (light [blonde, light brown], medium [medium brown, red], dark [dark brown, black]); typical application mechanism of hair dyes (salon, home kit, combination [both home kit and salon application]); total duration (years) of relaxer use (≤10 years, >10 years); early relaxer use (did not use before age 12, used before age 12); typical application mechanism of relaxers (salon, home kit, combination); and joint use of hair dyes and relaxers (user of hair dye only, user of relaxer only, user of both hair dye and relaxer). Reporting the application of hair dyes and relaxers as both at the salon and at home is hereafter referred to as 'combination application'.

Tumor clinicopathology data were abstracted from pathology records. Tumor grade was defined as grades 1 (well differentiated), 2 (moderately differentiated), and 3 (poorly differentiated). Tumor size (cm) was classified into three categories: <1.0 cm, 1.0–2.0 cm, and >2.0 cm. American Joint Committee on Cancer (AJCC) stage data was recorded as stages 0 through IV. Lymph node status was defined as node negative or node positive, based on the presence of cancer cells in axillary lymph nodes. We used surrogate classifications for ER status, PR status, and HER2 status, which were based on IHC expression of ER and PR, and overexpression of HER2 (by IHC and/or fluorescence in situ hybridization [FISH]). Of note, in WCHS and WCHFS, ER and PR status were classified as positive if ≥10% of cells demonstrated positive staining and negative if <10% of cells demonstrated positive staining (rather than using the 1% threshold that is used clinically (46)). Using the surrogate classifications for ER, PR, and HER2 status, we approximated breast tumor subtype into three mutually exclusive, clinically-recognized subtypes: luminal A (HR+/HER2−), HER2-positive (HR+ or HR−/HER2+), and TN (HR−/HER2−).

This study was conducted in accordance with the ethical principles of the Declaration of Helsinki and was approved by the Institutional Review Boards of all participating institutions. All study participants provided written informed consent prior to study enrollment.

Statistical Analysis

Participant sociodemographic information, hair product use characteristics, and tumor clinicopathology were described using summary statistics (frequencies and proportions for categorical variables and means and standard deviation for continuous variables). Ordinal, logistic or polytomous logistic regression models were used to estimate the odds ratios (OR) and 95% confidence intervals (CI) to describe associations between hair product use (hair dyes, chemical relaxers, or both) and tumor characteristics. Initially, we used unadjusted logistic regression models for those with only two outcomes (e.g., ER status) and unadjusted polytomous logistic regression models for tumor characteristics with more than two discrete outcomes (e.g., tumor size). We then fit multivariable models, adjusting for potential cofounders that were selected *a priori*, including race (except for the race-stratified analyses), age, BMI, family history of breast cancer, oral contraceptive use, education level (as a proxy for socioeconomic status), and mode of initial detection (as a proxy for access and utilization of mammography screening). In our models, the referent groups were as follows: 1) ‘never-users’ for regular hair dye use, duration of hair dye use, and typical shade of dye used; 2) ‘salon application’ for typical application of hair dyes or relaxers; 3) ‘never-users’ for regular relaxer use, duration of relaxer use, and early relaxer use; 4) ‘light hair dye shade’ for typical shade of dye; and 5) ‘never-users of both hair dyes and relaxers’ for joint use of hair dyes and relaxers. Bonferroni correction was used to address multiple comparisons. Cochran-Armitage trend tests were performed to evaluate trend effects of duration of exposure to hair dye and relaxer use on the outcome variables, as well as trends for the associations with tumor size and tumor grade. Primary analysis focused on associations in the overall sample and secondary analysis examined the associations of interest stratified by race and by ER status (shown in Supplementary Tables). Analyses

were done using R v3.6.1. All reported *P*-values are two-sided, and $P<0.05$ was considered statistically significant.

RESULTS

Select characteristics of the study sample

There were more Black women in the study sample (2,227 Black vs. 771 White) because the WCHS stopped recruiting White breast cancer cases in 2012, while enrollment of new Black breast cancer cases continued beyond 2012. The current analysis included White women diagnosed with breast cancer between 2001 and 2009 and Black women diagnosed with breast cancer between 2001 through 2018. Overall, the mean age at diagnosis was 53.3±10.6 years. Most demographic, clinical and reproductive characteristics differed by race, with the exception of age at menarche and history of oral contraceptive use (Table 1). As previously reported in WCHS (47), there were notable differences in breast tumor clinicopathologic features by race, indicating that Black women were more likely to be diagnosed with tumors that exhibited more aggressive phenotypes. This included more frequently having tumors that were poorly differentiated, >2.0 cm, ER−, lymph node positive, and TN subtype compared to White women.

Prevalence of regular use of permanent hair dye (35.5% vs. 62.1%, P<0.001) was lower and relaxer use was higher (88.1% vs. 7.7%, P<0.001) among Black than White women, respectively (Table 2). Significant racial differences were also observed for each hair product use characteristic examined. Notable differences included a larger proportion of White women reporting long-term use of permanent hair dye (>10 years) and more frequent use of salon application among White women compared to Black women. In terms of relaxer use, as previously reported in WCHS (13), a significantly larger proportion of Black women reported long-term use of relaxers and use of these products before age 12 years. Comparisons between users and non-users of hair dye and relaxer confirmed that age, race, education, and family history of breast cancer are potential confounders of the association between hair dye use and breast cancer, while race, education, BMI, family history of breast cancer, and history of oral contraceptive use are potential confounders for the associations of relaxer use and breast cancer (Supplementary Table 1).

Associations of hair product use characteristics with breast tumor clinicopathology

Permanent Hair Dye Use—No statistically significant associations were observed between regular use of permanent hair dye and any tumor clinicopathologic features (Table 3). However, we found that among women reporting >10 years of hair dye use, there appeared to be borderline significant increase in the odds of higher tumor grade, although the trend test was not significant. Notably, compared to salon only application, use of home kit only and combination (salon and home kit) application of permanent hair dyes were associated with increased odds of higher tumor grade and with larger tumor size. Only the association of combination application with increased odds of poorly differentiated tumor grade was statistically significant upon controlling for multiple comparisons (OR 2.27, 95% CI: 1.36–3.82), despite a statistically non-significant trend. In sensitivity analysis, this finding remained significant among women ≥50 years (OR 2.46, 95% CI: 1.36–4.47), while

among women <50 the estimate was imprecise (OR 2.68, 95% CI: 0.92–7.84). Typical hair dye shade used was not associated with breast tumor clinicopathologic features.

In race-stratified models, unexpectedly, among Black women reporting ≤10 years of hair dye use, there were significantly decreased odds of tumors >2.0 cm (OR 0.69, 95% CI: 0.53–0.89; Table 4). Use of permanent hair dye for >10 years, as well as home kit and combination application of hair dye were associated with increased odds of higher tumor grade. Home kit (OR = 2.22, 95% CI: 1.10–4.44) and combination application (OR = 2.46, 95% CI: 1.12–5.00) of dyes were positively associated with poorly differentiated tumors among Black women. Conversely, among White women (Table 5), there was a non-significant association between combination application of hair dyes with higher tumor grade. We also observed that among White women who reported using hair dye for >10 years, there were lower odds of positive lymph node status (OR = 0.46, 95% CI: 0.27–0.79), which was not observed among Black women.

Relaxer Use—Compared to non-use of relaxers, there appeared to be an inverse association between regular use and reduced odds of higher tumor grade (P-trend = 0.037), although the risk estimates did not reach statistical significance (Table 6). Overall, duration of relaxer use >10 years (1.0–2.0 cm: OR = 1.72, 95% CI: 1.04–2.87) and use of relaxers before age 12 (1.0–2.0 cm: OR = 1.65, 95% CI: 1.02–2.68) were significantly associated with larger tumor size, although the risk estimates for tumors >2.0 cm hovered near 1.00. Among women reporting relaxer use >10 years there was a significant positive trend for increasing tumor size (P-trend = 0.0086). Relaxer use before and after age 12 appeared to be associated with increasing tumor size (P-trends = 0.021 and 0.015, respectively). Compared to salon only application, home kit (1.0–2.0 cm: OR 1.29, 95% CI: 0.85–1.97 and >2.0 cm: OR 1.45, 95% CI: 0.92–2.29) and combination application of relaxer was associated with increased odds of larger tumor size (1.0–2.0 cm: OR 1.34, 95% CI: 0.93–1.94 and >2.0 cm: OR = 1.82, 95% CI: 1.23–2.69); only the association of combination application with tumors >2.0 cm remained significant after correction for multiple comparisons. Sensitivity analysis indicated that the association between combination application of relaxers with tumors >2.0 cm was consistent among women ≥50 years (OR 1.81, 95% CI: 1.07–3.07) and <50 years (OR 1.81, 95% CI: 1.01–3.27). Joint use of hair dye and relaxer was not significantly associated with any tumor clinicopathology feature.

Among Black women, compared to salon only application, home kit (1.0–2.0 cm: OR 1.31, 95% CI: 0.85–2.03 and >2.0 cm: OR 1.43, 95% CI: 0.90–2.27) and combination application (1.0–2.0 cm: OR 1.37, 95% CI: 0.94–1.99 and >2.0 cm: OR = 1.81, 95% CI: 1.22–2.88) of relaxers were associated with higher odds of larger tumors; again, only the association of combination application with tumors >2.0 cm remained significant after correction for multiple comparisons (Table 7). We were unable to assess associations of relaxer use characteristics with the outcomes of interest among White women due to their low prevalence of relaxer use.

Associations of hair dye and relaxer use with breast tumor clinicopathology, stratified by ER status—We also explored the associations of interest in analysis stratified by ER status. Among ER+ cases (Supplementary Table 2), we observed an inverse

association between regular hair dye use and both lymph node status and larger tumor size. Duration of hair dye use >10 years (moderately differentiated: OR 1.28, 95% CI: 0.87–1.87 and poorly differentiated: OR = 1.69, 95% CI: 1.12–2.56) and combination application of hair dye were associated with increased odds of higher tumor grade (moderately differentiated: OR = 1.76, 95% CI: 1.03–3.04 and poorly differentiated: OR = 2.98, 95% CI: 1.62–5.49). Among ER+ cases, no significant associations were observed for regular use, duration of relaxer use or with use before age 12. Combination application of relaxers was associated with increased odds of larger tumor size, but this association did not reach statistical significance upon correction for multiple comparisons.

Among ER− cases, regular use of relaxers was significantly associated with increased odds of positive lymph node status (OR 2.03, 95% CI: 1.11–3.86) (Supplementary Table 3). Relaxer use >10 years and use before age 12 were associated with increased odds of larger tumor size, HER2+ status, and positive lymph node status, although these associations were not significant upon correction for multiple comparisons. The association for combination application of relaxers with larger size was found among ER− cases as among ER+ cases. However, we also observed an inverse association between combination application of relaxers and positive lymph node status in ER− disease. Joint use of hair dyes and relaxers was associated with higher odds of positive lymph node status in ER− cases (OR 2.69, 95% CI: 1.15–6.80), which was not observed among ER+ cases (OR 0.67, 95% CI: 0.44, 1.02).

DISCUSSION

Hair dye and relaxer use has been shown to be associated with increased risk of breast cancer with estimates ranging from 10% to 70% greater risk (3, 6, 8, 13, 48). However, aside from earlier data from our group and others, which suggested differences in the associations of hair product use with breast cancer risk by ER status (6, 13, 26), no prior study has examined the associations of hair dye and relaxer use with breast tumor features including tumor grade, tumor size, receptor and lymph node status, and tumor subtype. This is the first step in assessing the potential impacts of these exposures on breast cancer prognostic indicators. In the current study, we demonstrated that, beyond ever vs. never use of permanent hair dyes and chemical relaxers, combination application of these hair products (having a history of both home kit application and salon application), longer duration of relaxer use, and relaxer use before age 12 years were associated with breast tumor clinicopathology. These findings generate new hypotheses about the potential impact of hair product use on breast cancer outcomes. We also conclude, based on our assessment of the exposures of interest, that crude measures of hair dye and relaxer use (i.e., ever vs. never) may be differentially associated with tumor characteristics, compared to more granular measures of use that potentially capture more cumulative measures of exposure (e.g., intensity). This warrants improvements in the classification of hair product exposures, especially hair dye, in future studies. We observed unexpected inverse associations in the analysis of ever-use and duration of hair dye use with tumor size and lymph node status, while combination application of hair dyes (compared to salon application only) were significantly associated with higher tumor grade, particularly among Black women. Similarly, duration and earlier use of relaxers, and combination application of relaxers

were associated with increased tumor size. But, our findings did not support an association between joint use of hair dyes and relaxers with more aggressive tumor clinicopathology.

Epidemiologic evidence supports a significant association between hair dye use, race, and increased risk of breast cancer (6, 8, 13). While in our prior case-control analysis of WCHS we reported a null association between hair dye use and breast cancer among Black and White women, and a positive association between use of dark hair dye shades and increased breast cancer risk among Black women only (OR 1.51, 95% CI: 1.20–1.90) (13), here we show that neither regular hair dye use nor dark shades of hair dye were associated with aggressive tumor features. Unexpectedly, regular hair dye use was observed to be inversely associated with tumor size, with associations restricted to Black women and to ER+ cases. This suggests that, in the examination of associations between hair dye use and breast tumor features, more granular measures of hair dye use are needed to fully understand associations with breast cancer risk and with clinicopathologic characteristics. For example, application type tended to be associated with more aggressive clinicopathological features, while ever-use generally was not, which could be an indication that compared to salon application, home kit and combination use (in particular) are important characteristics of hair dye use to consider. While the differences in association between crude and granular measures of hair dye use with tumor features requires further study, we also acknowledge that these differing associations could be attributed to women's inability to distinguish between use of permanent vs. semi-permanent hair dye, which could impact reported estimates of hair dye use within the study sample and the associations with our outcomes of interest.

As noted above, hair dye application type was associated with aggressive tumor features. Specifically, we found that combination application (vs. salon only application) was associated with higher tumor grade. Combination application was associated with greater odds of poorly differentiated tumors; these findings were limited to ER+ breast cancer cases and to Black women. Overall, these findings suggest that hair dye application type has a stronger impact on hormone responsive breast cancer, especially when diagnosed in Black women.

We previously reported that, among Black women, the use of darker shades of hair dye (vs. lighter shades) is associated with 1.50-times greater odds of developing breast cancer (irrespective of ER status) (13). Our current findings suggest that the shade of hair dye used may be differentially associated with breast tumor clinicopathology. Use of medium or dark hair dyes was associated with reduced odds of ER− tumors among Black women. Moreover, use of medium hair dye shades was associated with larger tumors among ER− cases. These findings are interesting and might suggest that compared to light shades, darker shades of hair dye might have more of an adverse impact on breast tumor features in hormone receptor positive than negative tumor subtypes.

Limited epidemiologic evidence supports a positive association between regular relaxer use and increased breast cancer risk (3, 6, 26), as well as other hormone-sensitive organs such as the uterus (49). Our observations in the overall sample showed that duration of relaxer use >10 years and use before age 12 were associated with 72% and 65% greater odds of tumor sizes 1.0–2.0 cm (compared to <1.0 cm), respectively. These

findings, along with the observation of significant trend of longer duration of hair dye use with ER− disease and earlier use of relaxer with larger tumors, point towards potential dose-dependent relationships that warrant further study. Evidence exists supporting a dose-response relationship between hair dye use and breast cancer risk (40); most recently, in 2020 Eberle et al. observed an increase in breast cancer risk associated with more frequent relaxer use (6). In ER− cases, compared to non-use, regular use of relaxer, >10 years of use, and use before age 12, as well as joint use of hair dye and relaxer were associated with significantly increased odds of positive lymph node status. This parallels the elevated risk for ER− invasive cancers and hair straightener use observed by Eberle and colleagues (6). These findings suggest that the intensity of exposure, due to longer duration of relaxer use and early use, may impact breast tumor clinicopathologic features. While duration of relaxer use >10 years was just shy of statistical significance, our findings highlight the need for accurately measuring intensity of exposure to hair products and other personal care products to understand their long-term effects on health outcomes. Future studies will need to confirm whether relaxer use habits closer to diagnosis and/or earlier in the life course are most relevant for associations with tumor phenotypes.

Combination application of relaxers (compared to salon application only) was significantly associated with increased odds of tumors >2.0 cm and the association remained strong independent of ER status, as well as among Black women. To our surprise, among women with ER− disease, combination application of relaxer was associated with lower odds of positive lymph nodes. Overall, all measures of relaxer use, crude or granular, were associated with more aggressive tumor features independent of breast cancer subtype. These findings are notable, particularly in comparison with findings of the large-scale Black Women's Health Study, which had not found any substantial increase in breast cancer risk (17). While the mechanistic roles of hair dye and relaxer use on breast cancer biology is unclear, one hypothesis is that EDCs (and other harmful chemicals) in these products induce adverse hormonal and carcinogenic influences (6, 13, 20, 50–54).

There were some notable differences between the manner in which Black and White women used hair products, as well as in their breast cancer phenotypes. Black women were much less likely to report use of permanent hair dye than White women, but much more likely to report using relaxers (with duration of use >10 years) than White women. Despite these important differences in hair product use and characteristics of use, there was generally a consistency in the association of combination application (salon and home kit application) of hair products with poorer tumor grade, larger tumor size, and with HER2+ tumor status. This further highlights the point regarding capturing intensity of hair product exposure to get a fuller picture of its contribution to clinical outcomes in breast cancer. The potential to clarify the associations of hair dye and relaxer use with tumor clinicopathology and subsequent long-term breast cancer prognosis will ultimately rely on improved measurement of these environmental exposures. We posit that a combination of home kit and salon application of hair dyes and relaxers might correlate with greater exposure intensity (55, 56) to these products over shorter periods of time, which might have more of an impact on breast cancer risk and phenotype when the exposure occurs before and during pubertal development (5, 32, 57). It is also possible that home kits have more hazardous chemicals than salon products or that women who use home kit application

might do so incorrectly (e.g., incorrect mixing of kit components, products left on the scalp longer than recommended, etc.), which might contribute to increased exposures to potentially harmful chemicals in the products used. Given our findings regarding duration of relaxer use and early use of relaxers, and building upon prior data, we hypothesize that the intensity of relaxer use might be the exposure needed to capture its effects on breast tumor clinicopathology and subsequently on breast cancer survival outcomes. This will require additional studies that are able to validly measure and characterize relaxer use exposures – frequency and intensity – and assess relationships among these exposures with long-term breast cancer prognosis.

As discussed in our earlier work (13), there are some limitations that should be considered in the interpretation of our findings. Recall bias (albeit non-differential in the current analysis of women with breast cancer) is of concern given that this study relied on participant's ability to accurately remember and report their use of hair dyes and relaxers over a long span of time, which could be decades among older participants. Given that the current analysis included cases only, it is possible that non-differential exposure misclassification could have biased our risk estimates towards the null as we do not anticipate that participants would have reported hair product use differently based on having more or less aggressive tumor features. Menopausal status at the time of diagnosis is another factor we could have considered in our analysis. Due to potential nuances within single categories of hair products (e.g., permanent vs. semi-permanent hair dyes), we are uncertain of participants' ability to accurately distinguish between types of hair products and we cannot speculate what affect this might have on the observed risk estimates. Additionally, changes in hair dye and/or chemical relaxer/straightening product formulations over time – which could not be assessed herein – and how these changes might have impacted the observed risk estimates is also a limitation. Another limitation was the relatively small sample size, particularly of White women, which reduced the precision of our estimates. Relatedly, low prevalence of relaxer use among White women (13) precluded exploration of some associations of interest. Nonetheless, our findings were generally consistent with regards to associations between longer duration of use, earlier use, and combination application of hair dyes and relaxers with increased odds of tumor features indicative of more aggressive phenotype. Despite these limitations, an important strength of this study was the large population-based design that included >2,000 Black women with breast cancer to assess the novel hypothesis that commonly used hair care products are associated with breast tumor clinicopathologic features. Collection of moderately detailed data on characteristics of hair product use and detailed information on confounding factors were additional strengths. Our findings also contribute to the generation of new hypotheses regarding potential impacts of hair dyes and relaxers on breast cancer outcomes, which warrants further study.

In summary, findings from this study provide preliminary data to support a relationship between characteristics of hair dye and relaxer use with breast tumor clinicopathology. These findings demonstrate that while crude ever vs. never measures of hair dye and relaxer use have linked these exposures with breast cancer risk, they may not adequately capture the granularity of hair product exposures needed to sufficiently assess the impacts of these exposures on breast cancer phenotypes and outcomes. Ideally, measures of chemical exposures assess dose, frequency, and duration. Applying a similar framework

of measurement to the assessment of hair dye and relaxer use might be most impactful in understanding associations with breast cancer outcomes. Moreover, such measurement may yield data that can contribute to the development of tailored actionable strategies for breast cancer risk reduction messaging by targeting particular high-risk hair dye and relaxer use patterns to mitigate breast cancer risk and poorer outcomes in the future.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Highlights

- This is the first study to examine the impact of characteristics of hair dye and relaxer use, including early use (before age 12), duration of use, typical application, and joint use of hair dyes and relaxers, on breast tumor features.
- Compared to salon only application, home kit and combination application (history of both home kit and salon application) of hair due were associated with 2-fold increased odds of poorly differentiated tumors, particularly among Black women.
- Compared to salon only application, combination application of relaxers was associated with 82% increased odds of larger tumors (>2.0 cm).
- Among women reporting relaxer use >10 years there was a significant positive trend for increasing tumor size.
- Joint use of hair dye and relaxer use was associated with more than 2-fold increased odds of positive lymph node status in ER− cases, which was not observed among ER+ cases.

Table 1.

Select characteristics of breast cancer cases, overall and by race, N = 2,998

	Overall (N = 2,998)	Black (n = 2,227)	White (n = 771)
Sociodemographic and clinical/reproductive characteristics	***n (%)***	***n (%)***	***n (%)***
Age (years), mean±SD	53.3±10.6	53.6±10.8	52.1±9.9
Education			
Less than 12th grade	257 (8.6)	235 (10.5)	22 (2.9)
High school graduate or equivalent	789 (26.3)	660 (29.7)	129 (16.7)
Some college	838 (28.0)	669 (30.0)	169 (21.9)
College graduate	639 (21.3)	404 (18.2)	235 (30.5)
Post-graduate	473 (15.8)	257 (11.6)	216 (28.0)
Insurance			
Medicare	375 (12.6)	310 (14.0)	65 (8.4)
Medicaid	335 (11.2)	307 (13.9)	28 (3.6)
Private	1,792 (60.2)	1,213 (54.9)	579 (75.3)
Uninsured	344 (11.6)	278 (12.5)	66 (8.7)
Other	132 (4.4)	101 (45.7)	31 (4.0)
Body mass index (kg/m^2), mean ± SD	30.5±7.1	31.7±7.0	27.1±6.4
Body mass index (kg/m^2)			
18.5–24.99	734 (24.4)	381 (17.1)	353 (45.8)
25.0–29.99	836 (27.9)	628 (28.2)	208 (27.0)
30.0–34.99	708 (23.6)	592 (26.6)	116 (15.0)
≥35.0	720 (24.1)	626 (28.1)	94 (12.2)
History of benign breast disease			
No	1,055 (35.4)	1,480 (66.9)	442 (57.8)
Yes	1,922 (64.6)	733 (33.1)	322 (42.2)
Initial mode of breast cancer detection			
Routine mammography	1,405 (47.1)	1000 (45.1)	405 (52.7)
Clinical breast exam/routine physical exam by healthcare provider	129 (4.3)	83 (3.7)	46 (6.0)
Self-detection/accidental discovery	1,034 (34.6)	794 (35.8)	240 (31.3)
Other	418 (14.0)	341 (15.4)	77 (10.0)
Family history of breast cancer			
No	2,435 (81.2)	1,843 (82.7)	592 (76.8)
Yes	563 (18.8)	384 (17.3)	179 (23.2)
Age at menarche (years), mean±SD	12.5±1.8	12.5±1.9	12.5±1.5
Parity			
Nulliparous	602 (20.1)	359 (16.1)	243 (37.1)
1–2	1,499 (50.0)	1,139 (51.1)	360 (54.9)
≥3	897 (29.9)	729 (32.8)	52 (8.0)
History of oral contraceptive use			
No	1,009 (33.7)	740 (33.3)	269 (35.0)

	Overall (N = 2,998)	Black (n = 2,227)	White (n = 771)
Sociodemographic and clinical/reproductive characteristics	***n (%)***	***n (%)***	***n (%)***
Yes	1,984 (66.3)	1,484 (66.7)	500 (65.0)
History of hormone replacement therapy			
No	2,455 (82.3)	1,880 (85.0)	575 (74.6)
Yes	528 (17.7)	332 (15.0)	196 (25.4)
Tumor clinicopathologic features			
Tumor grade			
Well differentiated	364 (14.7)	231 (12.2)	133 (22.9)
Moderately differentiated	1,042 (42.2)	786 (41.6)	256 (44.1)
Poorly differentiated	1,064 (43.1)	873 (46.2)	191 (33.0)
Tumor size			
<1.0 cm	1,416 (47.2)	994 (44.6)	422 (54.7)
1.0–2.0 cm	832 (27.8)	608 (27.3)	224 (29.1)
>2.0 cm	750 (25.0)	625 (28.1)	125 (16.2)
AJCC stage			
Stage 0	497 (18.9)	362 (18.4)	135 (20.6)
Stage I	1,014 (38.6)	705 (35.8)	309 (47.2)
Stage II	791 (30.1)	634 (32.2)	157 (24.0)
Stage III	272 (10.4)	227 (11.5)	45 (6.9)
Stage IV	52 (2.0)	43 (2.1)	9 (1.3)
ER status			
Positive	1,985 (73.7)	1,450 (71.3)	535 (80.9)
Negative	709 (26.3)	583 (28.7)	126 (19.1)
HER2 status			
Positive	483 (21.0)	380 (21.6)	103 (19.0)
Negative	1,783 (77.4)	1,355 (77.0)	428 (78.8)
Equivocal	37 (1.6)	25 (1.4)	12 (2.2)
PR status			
Positive	1,501 (56.6)	1,089 (54.1)	412 (64.4)
Negative	1,153 (43.4)	925 (45.9)	228 (35.6)
Lymph node status			
Positive	737 (31.5)	589 (32.8)	148 (27.2)
Negative	1,601 (68.5)	1,206 (67.2)	395 (72.8)
Tumor subtype			
Luminal A	1,311 (58.9)	955 (55.8)	365 (69.5)
HER2-positive	471 (21.2)	375 (21.9)	96 (18.8)
Triple-negative	442 (19.9)	382 (22.3)	60 (11.7)

Table 2.

Hair product use characteristics among of breast cancer cases, overall and by race, N = 2,998

	Overall (N = 2,998)	Black (n = 2,227)	White (n = 771)
Hair product use characteristics	***n (%)***	***n (%)***	***n (%)***
Regular hair dye use			
No	1,723 (57.7)	1,431 (64.5)	292 (37.9)
Yes	1,265 (42.3)	787 (35.5)	478 (62.1)
Duration of hair dye use			
Non-user	1723 (57.6)	1431 (64.5)	292 (37.9)
≤10 years of use	764 (25.6)	531 (23.9)	233 (30.3)
>10 years of use	501 (16.8)	256 (11.6)	245 (31.8)
Typical shade of hair dye used			
Non-user	1,723 (59.8)	1,431 (67.8)	292 (40.0)
Light (blonde, light brown)	362 (12.6)	182 (8.6)	180 (23.4)
Medium (medium brown, red)	378 (13.1)	180 (8.5)	198 (25.7)
Dark (dark brown, black)	419 (14.5)	320 (15.1)	99 (12.9)
Typical application of hair dyes			
Non-user	1,723 (60.2)	1,431 (67.7)	292 (38.9)
Salon	355 (12.4)	162 (7.7)	193 (25.7)
Home kit	434 (15.2)	282 (13.3)	152 (20.2)
Combination	351 (12.2)	238 (11.3)	113 (15.2)
Regular relaxer use			
No	943 (31.9)	263 (11.9)	680 (92.3)
Yes	2,011 (68.1)	1954 (88.1)	57 (7.7)
Duration of relaxer use			
Non-user	943 (31.9)	263 (11.9)	680 (92.3)
≤10 years of use	1851 (62.7)	1797 (81.0)	54 (7.3)
>10 years of use	160 (5.4)	157 (7.1)	3 (0.4)
Early relaxer use			
Non-user	943 (34.8)	263 (13.3)	680 (92.2)
User – did not use before age 12	1,585 (58.4)	1,536 (77.7)	49 (6.6)
User – used before age 12	185 (6.8)	177 (9.0)	8 (1.2)
Typical application of relaxers			
Non-user	943 (48.9)	263 (21.5)	680 (96.2)
Salon	285 (14.8)	271 (22.2)	14 (2.0)
Home kit	246 (12.8)	236 (19.3)	10 (1.4)
Combination	454 (23.5)	451 (37.0)	3 (0.4)
Joint use of hair dyes and relaxers			
Non-user of both hair dyes and relaxers	444 (15.1)	187 (8.5)	257 (34.9)
User of hair dyes only	496 (16.8)	74 (3.4)	422 (57.3)
User of relaxers only	1,250 (42.4)	1,236 (55.9)	14 (1.9)

	Overall (N = 2,998)	Black (n = 2,227)	White (n = 771)
Hair product use characteristics	***n (%)***	***n (%)***	***n (%)***
User of both hair dyes and relaxers	755 (25.6)	712 (32.2)	43 (5.84)

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Table 3.

Multivariable-adjusted associations of permanent hair dye use and characteristics of use with breast tumor clinicopathologic features in the overall study sample of breast cancer cases[a], N=2,998

	Regular hair dye use[b]	Duration of hair dye use[b]		Typical hair dye application[c]		Typical hair dye shade[d]	
		≤10 Years	>10 Years	Home Kit	Combination	Medium	Dark
Tumor feature	**OR (95% CI)**	**OR (95%CI)**	**OR (95%CI)**	**OR (95% CI)**	**OR (95% CI)**	**OR (95% CI)**	**OR (95% CI)**
Tumor grade							
Well differentiated	1.00 (REF)	1.00 (REF)	1.00 (REF)	1.00 (REF)	1.00 (REF)	1.00 (REF)	1.00 (REF)
Moderately differentiated	1.04 (0.81–1.34)	0.94 (0.70–1.25)	1.26 (0.88–1.82)	1.25 (0.79–1.99)	1.61 (0.97–2.67)	1.04 (0.64–1.68)	0.76 (0.47–1.23)
Poorly differentiated	1.07 (0.82–1.38)	0.90 (0.67–1.21)	1.46 (1.00–2.11)	1.41 (0.87–2.29)	2.27 (1.36–3.82)*	0.95 (0.59–1.55)	0.59 (0.36–0.97)
	P_{trend} = 0.46	P_{trend} = 0.43	P_{trend} = 0.75	P_{trend} = 0.23	P_{trend} = 0.13	P_{trend} = 0.89	P_{trend} = 0.77
Tumor size							
<1.0 cm	1.00 (REF)	1.00 (REF)	1.00 (REF)	1.00 (REF)	1.00 (REF)	1.00 (REF)	1.00 (REF)
1.0–2.0 cm	1.09 (0.91–1.30)	1.13 (0.92–1.38)	1.03 (0.80–1.34)	1.37 (0.97–1.95)	1.41 (0.98–2.03)	0.94 (0.67–1.32)	0.95 (0.67–1.34)
>2.0 cm	0.86 (0.71–1.04)	0.80 (0.63–1.00)	1.02 (0.77–1.35)	1.08 (0.72–1.63)	1.10 (0.72–1.68)	0.92 (0.62–1.36)	0.91 (0.61–1.34)
	P_{trend} = 0.59	P_{trend} = 0.32	P_{trend} = 0.78	P_{trend} = 0.11	P_{trend} = 0.054	P_{trend} = 0.76	P_{trend} = 0.96
ER status							
Negative	0.96 (0.80–1.15)	0.99 (0.80–1.22)	0.92 (0.70–1.21)	0.76 (0.51–1.10)	0.73 (0.49–1.07)	0.86 (0.60–1.24)	0.76 (0.53–1.08)
Positive	1.00 (REF)	1.00 (REF)	1.00 (REF)	1.00 (REF)	1.00 (REF)	1.00 (REF)	1.00 (REF)
		P_{trend} = 0.46	P_{trend} = 0.025				
HER2 status							
Negative	1.00 (REF)	1.00 (REF)	1.00 (REF)	1.00 (REF)	1.00 (REF)	1.00 (REF)	1.00 (REF)
Positive	1.09 (0.88–1.35)	1.24 (0.98–1.58)	0.78 (0.56–1.07)	0.99 (0.64–1.53)	1.05 (0.67–1.64)	1.11 (0.72–1.70)	1.00 (0.66–1.51)
		P_{trend} = 0.078	P_{trend} = 0.034				
Lymph node status							
Negative	1.00 (REF)	1.00 (REF)	1.00 (REF)	1.00 (REF)	1.00 (REF)	1.00 (REF)	1.00 (REF)
Positive	0.85 (0.70–1.03)	0.97 (0.78–1.21)	0.63 (0.47–0.84)*	1.12 (0.75–1.67)	0.77 (0.50–1.18)	1.21 (0.83–1.76)	0.83 (0.56–1.21)
		P_{trend} = 0.56	P_{trend} <0.001				
Tumor subtype							

	Regular hair dye use[b]	Duration of hair dye use[b]		Typical hair dye application[c]		Typical hair dye shade[d]	
		≤10 Years	>10 Years	Home Kit	Combination	Medium	Dark
Tumor feature	**OR (95% CI)**	**OR (95%CI)**	**OR (95%CI)**	**OR (95% CI)**	**OR (95% CI)**	**OR (95% CI)**	**OR (95% CI)**
Luminal A	1.00 (REF)	1.00 (REF)	1.00 (REF)	1.00 (REF)	1.00 (REF)	1.00 (REF)	1.00 (REF)
HER2-positive	1.11 (0.89–1.39)	1.28 (1.00–1.65)	0.79 (0.56–1.10	0.85 (0.54–1.35)	0.94 (0.59–1.50)	1.01 (0.64–1.58)	0.83 (0.54–1.29)
Triple-negative	0.99 (0.78–1.25)	1.04 (0.79–1.35)	0.93 (0.66–1.30)	0.74 (0.46–1.19)	0.62 (0.37–1.02)	0.85 (0.54–1.35)	0.65 (0.41–1.03)
		$P_{trend} = 0.15$	$P_{trend} = 0.017$				

[a] The multivariable-adjusted model included the following covariates: 1) family history of breast cancer, 2) oral contraceptive use, 3) education, 4) BMI, 5) age, 6) race, and 7) mode of detection.

[b] Never-users of hair dye composed the referent group.

[c] Those reporting salon application as the typical application of hair dyes composed the referent group.

[d] Those reporting typical use of light hair dye shades composed the referent group.

[*] Significant after correction for multiple comparisons (Bonferroni correction, P <0.01).

Table 4.

Multivariable-adjusted associations of hair dye use and characteristics of use with breast tumor clinicopathologic features among Black breast cancer cases[a]

	Regular hair dye use[b]	Duration of hair dye use[b]		Typical hair dye application[c]		Typical hair dye shade[d]	
		≤10 Years	≤10 Years	Home Kit	Combination	Medium	Dark
Tumor feature	**OR (95% CI)**	**OR (95% CI)**	**OR (95% CI)**	**OR (95% CI)**	**OR (95% CI)**	**OR (95% CI)**	**OR (95% CI)**
Tumor grade							
Well differentiated	1.00 (REF)	1.00 (REF)	1.00 (REF)	1.00 (REF)	1.00 (REF)	1.00 (REF)	1.00 (REF)
Moderately differentiated	1.02 (0.75–1.40)	0.92 (0.65–1.31)	1.29 (0.78–2.13)	1.64 (0.83–3.24)	1.66 (0.83–3.36)	1.20 (0.58–2.48)	1.08 (0.56–2.08)
Poorly differentiated	1.03 (0.76–1.41)	0.85 (0.60–1.21)	1.58 (0.95–2.62)	2.22 (1.10–4.44)	2.46 (1.21–5.00)	0.74 (0.36–1.52)	0.75 (0.39–1.42)
	P_{trend} = 0.94	P_{trend} = 0.73	P_{trend} = 0.70	P_{trend} = 0.40	P_{trend} = 0.38	P_{trend} = 0.68	P_{trend} = 0.83
Tumor size							
<1.0 cm	1.00 (REF)	1.00 (REF)	1.00 (REF)	1.00 (REF)	1.00 (REF)	1.00 (REF)	1.00 (REF)
1.0–2.0 cm	1.06 (0.86–1.31)	1.05 (0.83–1.33)	1.07 (0.77–1.48)	1.41 (0.86–2.31)	1.40 (0.86–2.29)	1.22 (0.74–2.00)	0.89 (0.57–1.38)
>2.0 cm	0.75 (0.60–0.94)	0.69 (0.53–0.89)*	0.91 (0.65–1.28)	1.08 (0.64–1.83)	0.95 (0.55–1.63)	0.92 (0.55–1.56)	0.77 (0.48–1.22)
	P_{trend} = 0.64	P_{trend} = 0.66	P_{trend} = 0.79	P_{trend} = 0.36	P_{trend} = 0.32	P_{trend} = 0.62	P_{trend} = 0.74
ER status							
Negative	0.94 (0.77–1.16)	0.97 (0.76–1.23)	0.91 (0.65–1.25)	0.77 (0.48–1.24)	0.62 (0.39–1.00)	0.64 (0.40–1.01)	0.59 (0.39–0.90)
Positive	1.00 (REF)	1.00 (REF)	1.00 (REF)	1.00 (REF)	1.00 (REF)	1.00 (REF)	1.00 (REF)
		P_{trend} = 0.81	P_{trend} = 0.29				
HER2 status							
Negative	1.00 (REF)	1.00 (REF)	1.00 (REF)	1.00 (REF)	1.00 (REF)	1.00 (REF)	1.00 (REF)
Positive	1.18 (0.93–1.50)	1.34 (1.02–1.75)	0.86 (0.57–1.27)	0.82 (0.48–1.43)	0.98 (0.57–1.70)	1.21 (0.69–2.15)	1.07 (0.66–1.77)
		P_{trend} = 0.026	P_{trend} = 0.28				
Lymph node status							
Negative	1.00 (REF)	1.00 (REF)	1.00 (REF)	1.00 (REF)	1.00 (REF)	1.00 (REF)	1.00 (REF)
Positive	0.92 (0.74–1.14)	1.02 (0.79–1.30)	0.72 (0.50–1.02)	1.11 (0.66–1.89)	0.88 (0.51–1.49)	1.04 (0.64–1.69)	0.79 (0.50–1.23)
		P_{trend} = 0.92	P_{trend} = 0.016				
Tumor subtype							

Tumor feature	Regular hair dye use[b]	Duration of hair dye use[b]		Typical hair dye application[c]		Typical hair dye shade[d]	
		≤10 Years	≤10 Years	Home Kit	Combination	Medium	Dark
	OR (95% CI)	OR (95% CI)	OR (95% CI)	OR (95% CI)	OR (95% CI)	OR (95% CI)	OR (95% CI)
Luminal A	1.00 (REF)	1.00 (REF)	1.00 (REF)	1.00 (REF)	1.00 (REF)	1.00 (REF)	1.00 (REF)
HER2-positive	1.19 (0.92–1.53)	1.35 (1.02–1.80)	0.87 (0.57–1.31)	0.72 (0.40–1.30)	0.79 (0.44–1.42)	1.03 (0.56–1.87)	0.88 (0.52–1.49)
Triple-negative	0.98 (0.76–1.27)	1.02 (0.76–1.37)	0.92 (0.62–1.36)	0.78 (0.44–1.38)	0.48 (0.26–0.89)	0.61 (0.34–1.10)	0.63 (0.38–1.05)
		P_{trend} = 0.057	P_{trend} = 0.31				

[a] The multivariable-adjusted model included the following covariates: 1) family history of breast cancer, 2) oral contraceptive use, 3) education, 4) BMI, 5) age and 6) mode of detection.

[b] Never-users of hair dye composed the referent group.

[c] Those reporting salon application as the typical application of hair dyes composed the referent group.

[d] Those reporting typical use of light hair dye shades composed the referent group.

Table 5.

Multivariable-adjusted associations of hair dye use and characteristics of use with breast tumor clinicopathologic features among White breast cancer cases[a]

	Regular hair dye use[b]	Duration of hair dye use[c]		Typical hair dye application[c]		Typical hair dye shade[d]	
		≤10 Years	>10 Years	Home Kit	Combination	Medium	Dark
Tumor feature	**OR (95% CI)**	**OR (95% CI)**	**OR (95% CI)**	**OR (95% CI)**	**OR (95% CI)**	**OR (95% CI)**	**OR (95% CI)**
Tumor grade							
Well differentiated	1.00 (REF)	1.00 (REF)	1.00 (REF)	1.00 (REF)	1.00 (REF)	1.00 (REF)	1.00 (REF)
Moderately differentiated	1.02 (0.66–1.59)	0.86 (0.51–1.44)	1.26 (0.73–2.15)	1.10 (0.59–2.08)	1.64 (0.78–3.46)	0.84 (0.44–1.61)	0.52 (0.26–1.05)
Poorly differentiated	1.11 (0.68–1.77)	0.97 (0.56–1.69)	1.23 (0.69–2.19)	0.90 (0.45–1.81)	2.05 (0.94–4.47)	1.27 (0.64–2.50)	0.51 (0.24–1.10)
	P_{trend} = 0.91	P_{trend} = 0.83	P_{trend} = 0.69	P_{trend} = 0.65	P_{trend} = 0.36	P_{trend} = 0.74	P_{trend} = 0.10
Tumor size							
<1.0 cm	1.00 (REF)	1.00 (REF)	1.00 (REF)	1.00 (REF)	1.00 (REF)	1.00 (REF)	1.00 (REF)
1.0–2.0 cm	1.14 (0.81–1.62)	1.35 (0.91–2.02)	0.95 (0.62–1.46)	1.34 (0.81–2.22)	1.44 (0.82–2.50)	0.76 (0.47–1.23)	1.09 (0.62–1.93)
>2.0 cm	1.36 (0.87–2.12)	1.36 (0.81–2.29)	1.27 (0.76–2.13)	1.13 (0.58–2.18)	1.43 (0.73–2.84)	0.95 (0.53–1.72)	1.35 (0.66–2.76)
	P_{trend} = 0.39	P_{trend} = 0.15	P_{trend} = 0.98	P_{trend} = 0.31	P_{trend} = 0.16	P_{trend} = 0.35	P_{trend} = 0.74
ER status							
Negative	1.04 (0.69–1.58)	1.08 (0.67–1.74)	0.97 (0.58–1.61)	0.74 (0.39–1.40)	0.95 (0.49–1.81)	1.33 (0.73–2.44)	1.44 (0.72–2.87)
Positive	1.00 (REF)	1.00 (REF)	1.00 (REF)	1.00 (REF)	1.00 (REF)	1.00 (REF)	1.00 (REF)
		P_{trend} = 0.79	P_{trend} = 0.76				
HER2 status							
Negative	1.00 (REF)	1.00 (REF)	1.00 (REF)	1.00 (REF)	1.00 (REF)	1.00 (REF)	1.00 (REF)
Positive	0.87 (0.56–1.37)	1.00 (0.59–1.66)	0.64 (0.36–1.13)	1.30 (0.63–2.71)	1.18 (0.54–2.54)	0.96 (0.50–1.87)	0.75 (0.32–1.67)
		P_{trend} = 0.79	P_{trend} = 0.049				
Lymph node status							
Negative	1.00 (REF)	1.00 (REF)	1.00 (REF)	1.00 (REF)	1.00 (REF)	1.00 (REF)	1.00 (REF)
Positive	0.62 (0.41–0.94)	0.79 (0.49–1.26)	0.46 (0.27–0.79)*	1.18 (0.60–2.29)	0.56 (0.26–1.18)	1.52 (0.83–2.79)	0.81 (0.36–1.74)
		P_{trend} = 0.47	P_{trend} = 0.0024				
Tumor subtype							

	Regular hair dye use[b]	Duration of hair dye use[c]		Typical hair dye application[c]		Typical hair dye shade[d]	
		≤10 Years	>10 Years	Home Kit	Combination	Medium	Dark
Tumor feature	**OR (95% CI)**	**OR (95% CI)**	**OR (95% CI)**	**OR (95% CI)**	**OR (95% CI)**	**OR (95% CI)**	**OR (95% CI)**
Luminal A	1.00 (REF)	1.00 (REF)	1.00 (REF)	1.00 (REF)	1.00 (REF)	1.00 (REF)	1.00 (REF)
HER2-positive	0.92 (0.57–1.49)	1.09 (0.64–1.87)	0.66 (0.36–1.21)	1.12 (0.51–2.43)	1.26 (0.57–2.80)	0.92 (0.46–1.85)	0.64 (0.27–1.49)
Triple-negative	1.05 (0.58–1.90)	1.12 (0.57–2.1)	1.04 (0.50–2.15)	0.63 (0.25–1.59)	1.06 (0.43–2.58)	1.47 (0.65–3.33)	0.70 (0.24–2.07)
		P_{trend} = 0.97	P_{trend} = 0.064				

[a] The multivariable-adjusted model included the following covariates: 1) family history of breast cancer, 2) oral contraceptive use, 3) education, 4) BMI, 5) age and 6) mode of detection.

[b] Never-users of hair dye composed the referent group.

[c] Those reporting salon application as the typical application of hair dyes composed the referent group.

[d] Those reporting typical use of light hair dye shades composed the referent group.

[*] Significant after correction for multiple comparisons (Bonferroni correction, P <0.01).

Table 6.

Multivariable-adjusted associations of relaxer use and characteristics of use with breast tumor clinicopathologic features in the overall study sample of breast cancer cases[a], N=2,998

	Regular relaxer use[b]	Duration of relaxer use[b]		Early relaxer use[b]		Typical relaxer application[c]		Joint use of hair dye and relaxer[d]
		≤10 Years	>10 Years	Did not use before age 12	Used before age 12	Home kit	Combination	
Tumor feature	**OR (95% CI)**	**OR (95%CI)**	**OR (95%CI)**	**OR (95%CI)**	**OR (95%CI)**	**OR (95% CI)**	**OR (95% CI)**	**OR (95% CI)**
Tumor grade								
Well differentiated	1.00 (REF)	1.00 (REF)	1.00 (REF)	1.00 (REF)	1.00 (REF)	1.00 (REF)	1.00 (REF)	1.00 (REF)
Moderately differentiated	0.77 (0.51–1.17)	0.77 (0.50–1.17)	0.94 (0.42–2.23)	0.79 (0.52–1.21)	0.92 (0.43–1.99)	0.84 (0.45–1.57)	0.83 (0.48–1.44)	0.70 (0.41–1.17)
Poorly differentiated	0.76 (0.49–1.16)	0.75 (0.49–1.15)	0.98 (0.44–2.18)	0.78 (0.51–1.21)	0.90 (0.42–1.93)	0.68 (0.36–1.27)	0.95 (0.55–1.64)	0.69 (0.41–1.18)
	P_{trend} = 0.037	P_{trend} = 0.050	P_{trend} = 0.20	P_{trend} = 0.051	P_{trend} = 0.16	P_{trend} = 0.97	P_{trend} = 0.82	P_{trend} = 0.38
Tumor size								
<1.0 cm	1.00 (REF)	1.00 (REF)	1.00 (REF)	1.00 (REF)	1.00 (REF)	1.00 (REF)	1.00 (REF)	1.00 (REF)
1.0–2.0 cm	1.11 (0.83–1.48)	1.11 (0.83–1.48)	1.72 (1.04–2.87)	1.22 (0.91–1.64)	1.65 (1.02–2.68)	1.29 (0.85–1.97)	1.34 (0.93–1.94)	1.11 (0.78–1.59)
>2.0 cm	0.88 (0.66–1.19)	0.90 (0.67–1.22)	1.03 (0.60–1.76)	1.03 (0.76–1.39)	1.03 (0.62–1.71)	1.45 (0.92–2.29)	1.82 (1.23–2.69) *	0.67 (0.46–0.99)
	P_{trend} = 0.16	P_{trend} = 0.31	P_{trend} = 0.0086	P_{trend} = 0.021	P_{trend} = 0.015	P_{trend} = 0.24	P_{trend} = 0.13	P_{trend} = 0.17
ER status								
Negative	1.18 (0.88–1.59)	1.22 (0.91–1.65)	0.80 (0.47–1.33)	1.24 (0.92–1.67)	0.83 (0.51–1.36)	0.87 (0.58–1.30)	0.80 (0.56–1.13)	1.08 (0.75–1.58)
Positive	1.00 (REF)	1.00 (REF)	1.00 (REF)	1.00 (REF)	1.00 (REF)	1.00 (REF)	1.00 (REF)	1.00 (REF)
		P_{trend} < 0.001	P_{trend} = 0.099					
HER2 status								
Negative	1.00 (REF)	1.00 (REF)	1.00 (REF)	1.00 (REF)	1.00 (REF)	1.00 (REF)	1.00 (REF)	1.00 (REF)
Positive	0.97 (0.70–1.36)	0.98 (0.71–1.37)	1.09 (0.61–1.93)	1.00 (0.72–1.41)	1.04 (0.60–1.78)	0.93 (0.58–1.49)	0.84 (0.56–1.26)	1.11 (0.73–1.70)
		P_{trend} = 0.47	P_{trend} = 0.35					
Lymph node status								
Negative	1.00 (REF)	1.00 (REF)	1.00 (REF)	1.00 (REF)	1.00 (REF)	1.00 (REF)	1.00 (REF)	1.00 (REF)
Positive	1.04 (0.77–1.40)	1.06 (0.78–1.43)	1.09 (0.66–1.81)	1.05 (0.77–1.43)	1.06 (0.65–1.71)	0.95 (0.62–1.45)	0.84 (0.58–1.21)	0.87 (0.60–1.25)
		P_{trend} = 0.078	P_{trend} = 0.0075					

	Regular relaxer use[b]	Duration of relaxer use[b]		Early relaxer use[b]		Typical relaxer application[c]		Joint use of hair dye and relaxer[d]
		≤10 Years	>10 Years	Did not use before age 12	Used before age 12	Home kit	Combination	
Tumor feature	**OR (95% CI)**	**OR (95%CI)**	**OR (95%CI)**	**OR (95%CI)**	**OR (95%CI)**	**OR (95% CI)**	**OR (95% CI)**	**OR (95% CI)**
Tumor subtype								
Luminal A	1.00 (REF)	1.00 (REF)	1.00 (REF)	1.00 (REF)	1.00 (REF)	1.00 (REF)	1.00 (REF)	1.00 (REF)
HER2-positive	1.00 (0.71–1.41)	1.02 (0.72–1.45)	0.87 (0.47–1.60)	1.04 (0.73–1.49)	0.82 (0.46–1.47)	0.87 (0.52–1.45)	0.80 (0.52–1.25)	1.16 (0.75–1.80)
Triple-negative	1.14 (0.79–1.64)	1.18 (0.82–1.70)	0.64 (0.34–1.20)	1.20 (0.83–1.73)	0.67 (0.37–1.23)	0.76 (0.46–1.26)	0.78 (0.50–1.19)	1.10 (0.69–1.75)
		P_{trend} = 0.052	P_{trend} = 0.25					

[a]The multivariable-adjusted model included the following covariates: 1) family history of breast cancer, 2) oral contraceptive use, 3) education, 4) BMI, 5) age, 6) race, and 7) mode of detection.

[b]Never-users of chemical relaxers/straighteners composed the referent group.

[c]Those reporting salon application as the typical application of relaxers composed the referent group.

[d]Those reporting no regular hair dye use and no regular relaxer use (i.e., never-users of both products) composed the referent group.

*Significant after correction for multiple comparisons (Bonferroni correction, P <0.01).

Table 7.

Multivariable-adjusted associations of relaxer use and characteristics of use with breast tumor clinicopathologic features among Black breast cancer cases[a]

	Regular relaxer use[b]	Duration of relaxer use[b]		Early relaxer use[b]		Typical relaxer application[c]		Joint use of hair dye and relaxer[d]
		≤10 Years	>10 Years	Did not use before age 12	Used before age 12	Home kit	Combination	
Tumor feature	**OR (95% CI)**	**OR (95% CI)**	**OR (95% CI)**	**OR (95% CI)**	**OR (95% CI)**	**OR (95% CI)**	**OR (95% CI)**	**OR (95% CI)**
Tumor grade								
Well differentiated	1.00 (REF)	1.00 (REF)	1.00 (REF)	1.00 (REF)	1.00 (REF)	1.00 (REF)	1.00 (REF)	1.00 (REF)
Moderately differentiated	0.86 (0.53–1.42)	0.86 (0.52–1.41)	0.74 (0.29–1.89)	0.88 (0.53–1.45)	0.79 (0.32–1.97)	1.03 (0.54–1.96)	0.89 (0.51–1.54)	0.72 (0.38–1.39)
Poorly differentiated	0.79 (0.48–1.30)	0.79 (0.48–1.30)	0.71 (0.28–1.78)	0.82 (0.50–1.36)	0.72 (0.29–1.77)	0.85 (0.44–1.63)	1.02 (0.59–1.77)	0.69 (0.36–1.32)
	P_{trend} = 0.69	P_{trend} = 0.66	P_{trend} = 0.86	P_{trend} = 0.68	P_{trend} = 0.76	P_{trend} = 0.75	P_{trend} = 0.78	P_{trend} = 0.53
Tumor size								
<1.0 cm	1.00 (REF)	1.00 (REF)	1.00 (REF)	1.00 (REF)	1.00 (REF)	1.00 (REF)	1.00 (REF)	1.00 (REF)
1.0–2.0 cm	1.16 (0.83–1.61)	1.13 (0.81–1.57)	1.75 (0.98–3.13)	1.31 (0.94–1.83)	1.60 (0.91–2.82)	1.31 (0.85–2.03)	1.37 (0.94–1.99)	1.16 (0.76–1.75)
>2.0 cm	0.89 (0.65–1.23)	0.89 (0.64–1.22)	0.95 (0.52–1.72)	1.03 (0.74–1.43)	0.93 (0.52–1.65)	1.43 (0.90–2.27)	1.81 (1.22–2.68)*	0.64 (0.42–0.97)
	P_{trend} = 0.47	P_{trend} = 0.62	P_{trend} = 0.024	P_{trend} = 0.20	P_{trend} = 0.050	P_{trend} = 0.24	P_{trend} = 0.15	P_{trend} = 0.75
ER status								
Negative	1.16 (0.84–1.60)	1.19 (0.87–1.65)	0.74 (0.42–1.31)	1.22 (0.89–1.69)	0.77 (0.44–1.33)	0.90 (0.59–1.36)	0.81 (0.57–1.15)	1.12 (0.75–1.70)
Positive	1.00 (REF)	1.00 (REF)	1.00 (REF)	1.00 (REF)	1.00 (REF)	1.00 (REF)	1.00 (REF)	1.00 (REF)
		P_{trend} = 0.52	P_{trend} = 0.96					
HER2 status								
Negative	1.00 (REF)	1.00 (REF)	1.00 (REF)	1.00 (REF)	1.00 (REF)	1.00 (REF)	1.00 (REF)	1.00 (REF)
Positive	1.07 (0.75–1.56)	1.07 (0.74–1.56)	1.36 (0.72–2.58)	1.08 (0.75–1.58)	1.41 (0.76–2.64)	0.95 (0.59–1.53)	0.84 (0.56–1.27)	1.27 (0.79–2.09)
		P_{trend} = 0.81	P_{trend} = 0.53					
Lymph node status								
Negative	1.00 (REF)	1.00 (REF)	1.00 (REF)	1.00 (REF)	1.00 (REF)	1.00 (REF)	1.00 (REF)	1.00 (REF)
Positive	1.07 (0.77–1.49)	1.07 (0.77–1.49)	1.13 (0.65–1.98)	1.06 (0.77–1.49)	1.06 (0.61–1.84)	0.96 (0.63–1.46)	0.85 (0.59–1.23)	0.92 (0.61–1.40)
		P_{trend} = 0.91	P_{trend} = 0.11					

	Regular relaxer use[b]	Duration of relaxer use[b]		Early relaxer use[b]		Typical relaxer application[c]		Joint use of hair dye and relaxer[d]
		≤10 Years	>10 Years	Did not use before age 12	Used before age 12	Home kit	Combination	
Tumor feature	**OR (95% CI)**	**OR (95% CI)**	**OR (95% CI)**	**OR (95% CI)**	**OR (95% CI)**	**OR (95% CI)**	**OR (95% CI)**	**OR (95% CI)**
Tumor subtype								
Luminal A	1.00 (REF)	1.00 (REF)	1.00 (REF)	1.00 (REF)	1.00 (REF)	1.00 (REF)	1.00 (REF)	1.00 (REF)
HER2-positive	1.07 (0.73–1.57)	1.08 (0.73–1.59)	1.06 (0.54–2.09)	1.10 (0.75–1.63)	1.07 (0.55–2.08)	0.90 (0.54–1.50)	0.81 (0.52–1.27)	1.32 (0.80–2.19)
Triple-negative	1.09 (0.74–1.61)	1.13 (0.76–1.66)	0.63 (0.32–1.35)	1.16 (0.79–1.71)	0.65 (0.33–1.26)	0.79 (0.47–1.32)	0.79 (0.52–1.22)	1.18 (0.72–1.94)
		P_{trend} = 0.85	P_{trend} = 0.77					

[a] The multivariable-adjusted model included the following covariates: 1) family history of breast cancer, 2) oral contraceptive use, 3) education, 4) BMI, 5) age and 6) mode of detection.

[b] Never-users of chemical relaxers/straighteners composed the referent group.

[c] Those reporting salon application as the typical application of relaxers composed the referent group.

[d] Those reporting no regular hair dye use and no regular relaxer use (i.e., never-users of both products) composed the referent group.

[*] Significant after correction for multiple comparisons (Bonferroni correction, P <0.01).