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Hair dye and chemical straightener use and breast cancer risk in a large US population of black and white women

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Abstract

Many hair products contain endocrine disrupting compounds and carcinogens potentially relevant to breast cancer. Products used predominately by black women may contain more hormonally-active compounds.

In a national prospective cohort study, we examined the association between hair dye and chemical relaxer/straightener use and breast cancer risk by race.

Sister Study participants (N=46,709), women ages 35–74, were enrolled between 2003–2009, and had a sister with breast cancer but were breast cancer-free themselves. Enrollment questionnaires included past 12-month hair product use. Cox proportional hazards models estimated adjusted hazard ratios (HRs) and 95% confidence intervals (95% CIs) for the association between hair products and breast cancer; effect measure modification by race was evaluated.

During follow-up (mean=8.3 years), 2,794 breast cancers were identified. 55% of participants reported using permanent dye at enrollment. Permanent dye use was associated with 45% higher breast cancer risk in black women (HR=1.45, 95% CI: 1.10–1.90), and 7% higher risk in white women (HR=1.07, 95% CI: 0.99–1.16) (heterogeneity p=0.04). Among all participants, personal straightener use was associated with breast cancer risk (HR=1.18, 95% CI 0.99–1.41); with higher risk associated with increased frequency (p for trend=0.02). Non-professional application of semi-permanent dye (HR=1.28, 95% CI 1.05–1.56) and straighteners (HR=1.27, 95% CI 0.99–1.62) to others was associated with breast cancer risk.

We observed a higher breast cancer risk associated with any straightener use and personal use of permanent dye, especially among black women. These results suggest that chemicals in hair products may play a role in breast carcinogenesis.

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Conflicts of Interest: None declared.

Keywords

breast cancer; hair dye; chemical straighteners; hair products; personal care products

Background

In the United States, breast cancer incidence remains high for all women, and appears to be increasing for non-Hispanic Black women to the point of possible convergence with non-Hispanic white women.(1,2) Despite the similar trends in incidence, racial disparities persist with black women more likely to be diagnosed with aggressive tumor subtypes and die after a breast cancer diagnosis.(3–6) Understanding potentially modifiable breast cancer risk factors, especially those that may contribute to racial disparities, is central to identifying potential targets to reduce risk.

Hair dye use is very common; it has been estimated that more than one-third of women above the age of 18 in the United States use hair dye.(7) Hair products contain more than 5,000 chemicals(7,8), including those with mutagenic and endocrine disrupting properties such as aromatic amines.(9–11) Dye constituents, such as 2,4-diaminoanisole sulfate and para-Phenylenediamine, have been found to induce tumors in the mammary gland of rats. (12,13) Other aromatic amines including 4-aminobiphenyl-(ABP) can reach breast tissue; women who used hair dye in the past year were 8 times more likely to have ABP-DNA adducts in breast ductal epithelial cells.(9,14) Chemical treatments used to permanently or semi-permanently straighten or relax hair (hence forth referred to as straighteners) contain a mixture of chemicals, including formulations in which the carcinogen formaldehyde is an active ingredient.(15,16)

Prior findings on the association between hair dye use and breast cancer have been inconsistent; while a few studies have reported a positive association(17–20), many concluded that there was no elevated risk.(10,17,20–26) However, recently published case-control studies reported risk increases in excess of 25% for hair dye use in association with breast(18,19) and bladder cancer.(27) Fewer studies have considered the risk associated with straighteners, which are used predominately by women of African descent.(18,28,29) Hair product constituents vary depending on whether they are marketed to black or white women; studies suggest that products designed for use by black women may contain more endocrine disrupting chemicals.(30–32) Additionally, personal care product use patterns vary by race and thus differences in exposure to chemicals through hair products may contribute in part to racial disparities in breast cancer incidence.(30,33–37)

In this study, we evaluated the association of hair dye and straightener use with breast cancer in a large, prospective cohort of US women. We hypothesized that risk would be higher among women who used hair dye and straighteners and would vary by race, with black women having higher risk.

Methods

Study population

The previously described prospective Sister Study cohort enrolled 50,884 women aged 35–74 living in the United States (including Puerto Rico) from 2003–2009.(38) Women were eligible to participate if they had no history of breast cancer but had at least one sister who had been diagnosed with breast cancer. Participants answered structured questionnaires and computer-assisted telephone interviews at the time of enrollment. A trained examiner measured height and weight during a home visit. Participants provided annual updates to document health changes and completed detailed follow-up assessments every three years. Response rates have remained over 90% throughout study follow-up.(39)

All study participants provided written informed consent. The Sister Study was approved by the institutional review board of the National Institute of Health. This report includes follow up through September 15th, 2016 (Data Release 6.0).

Breast cancer outcome ascertainment

Participants reported incident breast cancer diagnoses in annual health updates, during follow-up surveys or by calling the Sister Study helpline. Following self-reported diagnoses, cases granted the release of medical records to confirm the diagnosis and ascertain further details, including estrogen receptor (ER) status and staging. Estrogen receptor responsiveness was available for 87.4% of invasive breast cancers. Tumors with positive or borderline results were classified as ER positive. Medical records were available for over 80% of cases. When medical record data was not available, we used self-reported data. Agreement between self-reported tumor characteristics and those from the medical record is high; the positive predictive value for ER positive breast cancer is 99.1%.(40)

Cases were defined as women diagnosed with an invasive breast cancer or ductal carcinoma *in situ* (DCIS). Women diagnosed with breast cancer prior to completion of all required enrollment activities were excluded (n=62). We considered whether associations varied by the extent of the tumor (invasive vs. DCIS), ER status, or menopausal status at diagnosis. When considering ER status, we limited to invasive cases as ER status was less commonly determined for *in situ* disease.

Exposures and Covariate Assessment

Current hair dye and straightener use, defined as use in the 12 months before enrollment, was assessed by questionnaire and was completed by 47,650 participants. Participants reported their frequency of personal use of permanent hair dye, semi-permanent hair dye, temporary dye, and straighteners in the 12 months before enrollment. Frequency was reported as "Did not use," "1–2 times per year," "Every 3–4 months," "Every 5–8 weeks," "Once a month" and "More than once a month". Additionally, participants reported their frequency of non-professional application of permanent dye, semi-permanent dye, and straighteners to others in the 12 months before enrollment. Current hair dye and straightener exposures were summarized as dichotomous variables - "Did not use in the past 12 months" vs. "Any use in the past 12 months" – and based on reported frequency of use – "Did not use

in the past 12 months", "Used 1–2 or 3–4 times in the past 12 months", or "Used every 5–8 weeks or once a month or more in the past 12 months".

Women that reported current permanent and semi-permanent dye use were asked whether they had used dark colors (black, brown, auburn/dark red), light colors (blonde, light red) or both. All participants reported duration of permanent and semi-permanent hair dye personal use as "Did not use", "Less than 5 years", "5–9 years", or "10 or more years".

Covariate information, including demographics, socioeconomic status and reproductive history, was obtained from participants during the enrollment telephone interview. Menopausal status and age at menopause were assessed at enrollment and updated during follow-up by asking about the timing of their last menstrual period and history of hysterectomy or oophorectomy.

Statistical analysis

We conducted descriptive analyses evaluating participant characteristics by current permanent dye use. We used Cox proportional hazards models to estimate hazard ratios (HRs) and 95% Confidence Intervals (CIs) for the association between dye and straightener use and breast cancer risk. For the Cox model, age was the timescale with follow-up beginning at enrollment and person-time accrued until breast cancer diagnosis or censoring event (defined as age of last follow-up or death). We tested for a linear trend for frequency of use with a chi-square test for the ordinal characterization of the variable. Participants diagnosed with lobular carcinoma *in situ* were censored in all analyses. The proportional hazards assumption was assessed using a likelihood ratio test to compare models with and without interaction terms between each covariate and time with an $\alpha=0.05$. There was no evidence of time-variant associations.

Confounders were identified using a directed acyclic graph.[41] All models were adjusted for age at menarche (continuous), enrollment menopausal status (premenopausal, postmenopausal), race and ethnicity (Non-Hispanic White, Black, Hispanic or Other), educational attainment (high school degree or equivalent or less, some college, bachelor's degree or higher), body mass index (<25 kg/m^2, 25–30 kg/m^2, >30 kg/m^2), smoking history (never, former, or current smoker), ever oral contraceptive use, parity (0–1 births, 2 births, 3 or more births) and age at first birth (nulliparous, <23, 23–27,>27). All women who self-reported black race, regardless of ethnicity, were classified as black. There was limited missing covariate data ($<2\%$) so we conducted a complete case analysis limiting to those without missing information on the a priori confounders. The final sample size was N=46,709.

Effect measure modification on the multiplicative scale was assessed using a likelihood ratio test to compare models with and without a cross-product term for race and the exposure variables. Stratum-specific estimates were obtained for black and non-Hispanic white participants. Stratum-specific estimates were not estimated for women classified as non-black Hispanic or other race due to small sample size and limited power.

When considering associations by ER status, women diagnosed with another type of breast cancer (e.g., ER- when the outcome of interest was ER+) were censored at the time of diagnosis. When considering associations by menopausal status at diagnosis, person-time was stratified by menopausal status. Women became at risk for postmenopausal breast cancer at enrollment or age at menopause, whichever was later. Women who were premenopausal at enrollment were censored at time of menopause for premenopausal breast cancer.

Sensitivity analyses included excluding women who had ever worked in a hair salon, mutually-adjusting the associations for straightener and permanent hair dye use, including additional adjustment for history of hormone replacement therapy and alcohol use and testing for effect measure modification by BMI. All analyses were completed using SAS 9.4 (Cary, North Carolina).

Data availability

Data used in this analysis may be requested through the Sister Study data management system; information on requesting data can be found at https://sisterstudy.niehs.nih.gov/English/data-requests.htm

Results

There were 2,794 incident breast cancer cases reported in 386,338 person-years. The average length of follow up was 8.3 years. Permanent hair dye use was common with 55% of women reporting use in the 12 months before enrollment. Compared to women who did not use permanent dye, women who used permanent dye tended to be younger, had fewer years of education, were more likely to currently smoke cigarettes and more likely to have used oral contraceptives (Table 1). Black women, postmenopausal women, and those with fewer children were less likely to have used permanent dye. Permanent dye use did not notably differ based on BMI or age at menarche.

Permanent dye use was related to breast cancer risk in the total sample. Compared to non-use, the hazard ratio for breast cancer was 1.09 for any current permanent dye use (95% CI: 1.01–1.17) (Table 2). This association did not vary by frequency of use. Compared to non-use, use of light-colored dye (HR =1.12, 95% CI: 1.02–1.23) and dark-colored dye (HR=1.08, 95% CI: 0.98–1.19) were associated with higher breast cancer risk. Associations did not vary with years of use. While semi-permanent dye use was not associated with risk, there was an association with non-professional application of semi-permanent dye to others (HR=1.28, 95% CI: 1.05–1.56). This risk was positively related to increasing frequency (p for trend=0.02). Temporary dye use was not associated with breast cancer risk. Associations for all exposures were similar for invasive breast cancer and DCIS (data not shown).

Associations with hair dye use tended to vary by race, especially for permanent dye (heterogeneity p=0.04) (Table 3). In black women, any permanent dye use in the 12 months before enrollment was associated with a 45% higher breast cancer risk (HR=1.45, 95% CI: 1.10–1.90). Increased frequency of use was positively associated with risk (p for trend=0.006); black women who used dye at least every 5–8 weeks had a 60% higher breast

cancer risk (95% CI: 1.11–2.30). The association with permanent dye use among black women was evident for both dark-colored dye (HR=1.51, 95% CI: 1.12–2.05) and, although less precise, light-colored dye (HR=1.46, 95% CI 0.91–2.34). Among white women, breast cancer risk was associated with use of light-colored permanent dye (HR=1.12, 95% 1.01–1.23) but not dark dye (HR=1.04, 95% 0.94–1.16).

Current straightener use (9.9% in total sample) varied by race, with 74.1% of black women reporting any use compared to 3.0% of non-Hispanic white women. Overall, straightener use in the 12 months before enrollment was associated with 18% higher breast cancer risk (95% CI: 0.99–1.41) (Table 2). More frequent straightener use was associated with higher risk (p for trend=0.02); women who used straighteners at least every 5–8 weeks had a 31% higher breast cancer risk (95% CI: 1.05–1.63). Similarly, a higher risk was evident for non-professional application of straighteners to others (HR=1.27, 95% CI: 0.99–1.62). The risk associated with straightener use did not notably vary by race and was evident for both Non-Hispanic white and black women (p=0.8).

We observed little evidence of heterogeneity by menopausal status at diagnosis. However, we did note a higher risk of premenopausal breast cancer (HR=1.30, 95% CI: 1.04–1.62) associated with light dye use (Supplemental Table 1). The association for non-professional application of semi-permanent dyes (HR=1.35, 95%CI 1.08–1.69), and personal use (HR=1.26, 95%CI 1.02–1.55) and application to others (HR=1.34, 95%CI: 0.99–1.791) of straighteners was most evident for postmenopausal breast cancer.

Although we had limited power to detect differences by ER-status (Supplemental Table 2), overall the risk associated with both permanent hair dye and straightener use appeared to be elevated for ER- invasive breast cancer compared to ER+ invasive breast cancer.

Neither excluding women who had ever worked in hair salons (N =1,616), nor adjusting for alcohol and hormone replacement therapy use materially changed results. There was no evidence of modification by BMI. Mutual adjustment for permanent dye and straightener use did not notably change the findings (data not shown).

Discussion

In this large prospective US-based study, we evaluated the relationship between hair dye and straightener use with breast cancer risk and found that women who used permanent dye or straighteners, or applied straighteners to others, in the 12 months before enrollment were at a higher breast cancer risk. The association with permanent hair dye was particularly evident in black women, for whom we observed a 45% higher breast cancer risk. Overall, these results support the hypothesis that hair dye and straightener use, which are highly prevalent exposures, could play a role in breast carcinogenesis.

The strength of association observed for permanent dye use among black women is consistent with toxicological assessments that report higher concentrations of estrogens and endocrine disrupting compounds in hair products marketed to black women.(30,31,33,42,43) Previous studies on hair dye use and breast cancer risk, including most that found no association, have largely been limited to white women.(10,17,20–23,26) Our findings are

consistent with those recently reported by the Women's Circle of Health Study (WCHS) who observed a very similar increase in risk (~50%) for use of dark dyes and a higher risk with increased frequency of permanent dye use among African-American women.(18) The WCHS study assessed exposure retrospectively and thus, could not rule out the possibility of recall bias.

We observed a 9% higher breast cancer risk for permanent dye use in all women but little to no associated risk for semi-permanent or temporary dye use. These findings are consistent with biological plausibility of differences in constituents and binding mechanisms between types of dye; namely, permanent dyes contain higher concentrations of aromatic amines.(43) Despite the estimated lower concentrations of oxidizing agents present in semi-permanent dyes, we did observe an association between non-professional application of semi-permanent dyes and breast cancer risk. At-home kits contain gloves, but potential absorption on hands and forearms, inhalation of toxic chemicals, and residual agents remaining on surfaces or in the air in poorly ventilated settings introduce several mechanisms for exposure.

The higher breast cancer risk observed in women who used straighteners is consistent with recent findings from both the Ghana Breast Health Study (GBHS) and WCHS.(18,29) Notably, these findings contrast null association observed in the Black Women's Health Study, which assessed exposure in the mid-1990s. However, this discrepancy may reflect changes in chemical formulation of popular straighteners between studies.(28) Historically, active ingredients in straighteners included sodium hydroxide and thioglycolic acid salts, neither of which have identified carcinogenic effects in humans.(18) In the early 2000s Brazilian Keratin Treatments (BKTs), which contain formaldehyde, a known carcinogen, (16) or one of its derivatives that reacts with keratin when heated, were introduced to global markets. Our finding is the first estimate of the association between straightener use and breast cancer from a prospective cohort that assessed exposure after the introduction of formaldehyde-containing straighteners to US markets.

Our findings for straightener use and ER status are remarkably similar to those reported by Llanos et al.(18) They also reported no association between personal straightener use and ER+ breast cancer and higher, but not significant, odds of ER- and triple negative breast cancer in African-American women. Their exposure captured ever use of any straightener reported over a similar time period, 2002–2014. Both studies were limited in number of ER-cases; future research that is better powered to estimate the risk associated with ER- breast cancers should be considered.

We were not able to evaluate the formulation of the hair dyes or straighteners assessed, nor are they reliably documented on labels(31) which is a limitation. By design, all study participants have a family history of breast cancer, which may limit the generalizability of these findings. However, this would not impact the internal validity of the study as it would not bias our estimates of the association between hair dye and straightener use and breast cancer risk. Although our study was prospective, limiting the possibility of recall bias, the potential for recall error remains. Though detailed exposure assessment was limited to the prior year to maximize recall, participants may have had difficulty differentiating between

types of dye (permanent, semi-permanent and temporary). Further, hair product use throughout follow-up was not considered. Future studies that are powered to robustly evaluate the possibility of differences by race and tumor subtype are needed. The consideration of detailed exposure information on hair dye and straightener use in a population of both black and white women was an important strength of this study. Further, our exposure collection time period allowed for assessment of more modern levels and types of exposure which may be particularly important given the change in popular straighteners.

In conclusion, these findings from a large, geographically-diverse prospective cohort with a sufficient sample size to separately evaluate results for white and black women provide evidence to support the relationship of hair dye and straightener use with breast cancer risk and highlight potential differences in associations by race. As hair dye and straighteners are common exposures, these findings have the potential for substantial public health impact.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgements:

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Novelty and Impact Statement:

This study evaluates the relationship between hair dye and chemical straightener use and breast cancer risk in a large prospective cohort using detailed exposure assessment including frequency and duration of use. These are common exposures; >50% reported hair dye use and almost 75% of black women reported straighter use in the past year. Findings indicate a higher breast cancer risk with use or application of chemical straighteners and permanent dye use, especially in black women.

Table 1:

Characteristics of the study population stratified by permanent hair dye use in the 12 months before enrollment, Sister Study 2003–2009.

Participant Characteristics	No permanent hair dye use N=20,822		Any permanent hair dye use N=25,887	
	N	%	N	%
Age at baseline (years), mean ±SD	56.9 ± 9.3		54.7 ± 8.5	
Age at menarche (years), mean ±SD	12.6 ± 1.5		12.7 ± 1.5	
Race/ethnicity				
Non-Hispanic White	17,368	83.4%	21,893	84.6%
Black	2,388	11.5%	1,699	6.6%
Hispanic	553	2.7%	1,588	6.1%
Other	513	2.5%	707	2.7%
Highest education				
High School or less	2,979	14.3%	4,191	16.2%
Some college	6,412	30.8%	9,241	35.7%
Bachelor's degree or more	11,431	54.9%	12,455	48.1%
Body Mass Index				
Normal/underweight	7,998	38.4%	9,900	38.2%
Overweight	6,460	31.0%	8,398	32.4%
Obese	6,364	30.6%	7,589	29.3%
Smoking Status				
Never	12,281	59.0%	14,029	54.2%
Past	7,133	34.3%	9,519	36.8%
Current	1,408	6.8%	2,339	9.0%
Enrollment Menopause status				
Premenopausal	6,249	30.0%	9,408	36.3%
Postmenopausal	14,573	70.0%	16,479	63.7%
Oral Contraceptive Use				
Never	3,820	18.4%	3,611	14.0%
Ever	17,002	81.7%	22,276	86.1%
Parity				
0–1 child	7,132	34.3%	8,047	31.1%
2 children	7,255	34.8%	10,002	38.6%
3 + children	6,435	30.9%	7,838	30.3%
Age at first birth				
Nulliparous	4,208	20.2%	4,232	16.4%
< 23 years old	6,408	30.8%	8,415	32.5%
23 – 27 years old	4,786	23.0%	6,188	23.9%
27 +	5,420	26.0%	7,052	27.2%

Table 2:

Hair dye and straightener exposure in the 12 months prior to enrollment and incident breast cancer, Sister Study, 2003–2009.

	Person-years	Events	Age-adjusted HR (95% CI)	Adjusted HR[*] (95% CI)
		2,794		
Permanent hair dye				
Personal use in the 12 months before enrollment				
No use [†]	173,213	1,235	Ref	Ref
Any use	213,125	1,559	1.07 (1.00, 1.16)	1.09 (1.01 1.17)
<4 times per year	89,931	634	1.07 (0.97, 1.17)	1.08 (0.98, 1.19)
Every 5–8 weeks, 1+ per month	123,194	925	1.08 (0.99, 1.18)	1.09 (1.00, 1.19)
p for trend				0.05
Dye color				
None	173,213	1,235	Ref	Ref
Light colors only	92,847	713	1.10 (1.00, 1.21)	1.12 (1.02, 1.23)
Dark colors only	94,908	683	1.07 (0.97, 1.18)	1.08 (0.98, 1.19)
Light and dark colors	23,009	144	0.95 (0.80, 1.14)	0.96 (0.81, 1.14)
Years of personal use				
None	135,033	965	Ref	Ref
< 5	63,995	458	1.07 (0.96, 1.20)	1.07 (0.96, 1.20)
5 or more	182,209	1,340	1.04 (0.96, 1.13)	1.05 (0.96, 1.14)
Applied to others				
No use [†]	357,754	2,606	Ref	Ref
Any use	28,585	188	0.97 (0.84, 1.13)	0.99 (0.85, 1.15)
<4 times per year	24,012	160	0.99 (0.85, 1.17)	1.01 (0.86, 1.19)
Every 5–8 weeks, 1+ per month	4,573	28	0.86 (0.59, 1.25)	0.88 (0.61, 1.28)
p for trend				0.7
Semi-permanent dye				
Personal use in the 12 months before enrollment				
No use [†]	315,173	2,311	Ref	Ref
Any use	71,165	483	0.96 (0.87, 1.05)	0.96 (0.87, 1.06)
<4 times per year	43,032	295	0.99 (0.88, 1.12)	0.99 (0.88, 1.12)
Every 5–8 weeks, 1+ per month	28,133	188	0.91 (0.78, 1.05)	0.91 (0.78, 1.06)
p for trend				0.3
Dye color				
None	315,173	2,311	Ref	Ref
Light colors only	20,860	145	0.94 (0.79, 1.11)	0.95 (0.80, 1.13)
Dark colors only	42,236	282	0.95 (0.84, 1.08)	0.96 (0.84, 1.09)
Light and dark colors	3,869	21	0.79 (0.51, 1.21)	0.79 (0.51, 1.21)
Years of personal use				
None	270,992	2,026	Ref	Ref

	Person-years	Events	Age-adjusted HR (95% CI)	Adjusted HR* (95% CI)
< 5	54,574	355	0.90 (0.80,1.01)	0.90 (0.80,1.01)
5 or more	52,540	356	0.89 (0.80,1.00)	0.90 (0.80,1.00)
Applied to others				
No use[†]	373,614	2,689	Ref	Ref
Any use	12,724	105	1.24 (1.02, 1.51)	1.28 (1.05,1.56)
<4 times per year	10,794	88	1.24 (1.00, 1.53)	1.27 (1.03,1.58)
Every 5–8 weeks, 1+ per month	1,930	17	1.26 (0.78, 2.04)	1.31 (0.81, 2.12)
p for trend				0.02
Temporary dyes (rinses)				
Personal use in the 12 months before enrollment				
No use	356,833	2,573	Ref	Ref
Any use	29,506	221	1.04 (0.90,1.19)	1.05 (0.91,1.21)
Chemical straighteners				
Personal use in the 12 months before enrollment				
No use[†]	351,502	2,543	Ref	Ref
Any use	34,837	251	1.09 (0.95,1.24)	1.18 (0.99,1.41)
<4 times per year	16,279	107	0.98 (0.81, 1.19)	1.07 (0.86, 1.34)
Every 5–8 weeks, 1+ per month	18,558	144	1.18 (0.99, 1.39)	1.31 (1.05, 1.63)
p for trend				0.02
Applied to others				
No use[†]	376,147	2,716	Ref	Ref
Any use	10,192	78	1.20 (0.96,1.51)	1.27 (0.99,1.62)
<4 times per year	7,619	62	1.28 (0.99,1.65)	1.35 (1.03,1.77)
Every 5–8 weeks, 1+ per month	2,573	16	0.97 (0.59, 1.59)	1.03 (0.62,1.70)
p for trend				0.2

*
models adjusted for age, race, education, ever oral contraceptive use (OC), parity, age at first birth, smoking status, BMI, age at menarche, menopausal status.

†For hazard ratio estimates associated with personal use in the 12 months before enrollment and application to others in the 12 months before enrollment, "No use" is the referent category for "Any use". For frequency of use, "No use" is also the referent category for "<4 times per year" and "Every 5 weeks, 1+month" and the p for trend is provided.

Table 3:

Hair dye and straightener exposures and incident breast cancer in non-Hispanic white and all black women, Sister Study 2003–2009.

	Non-Hispanic White			Black		
	Person-Years	Events	Adjusted HR (95% CI)	Person-Years	Events	Adjusted HR (95% CI)
		2,402			208	
Permanent hair dye						
Personal use in the 12 months before enrollment						
No use [†]	147,144	1,064	Ref	17,671	106	Ref
Any use	183,378	1,338	1.07 (0.99,1.16)	12,491	102	1.45 (1.10,1.90)
<4 times per year	74,915	524	1.06 (0.95,1.18)	8,218	62	1.36 (0.99,1.87)
Every 5–8 weeks, 1+ per month	108,464	814	1.08 (0.98,1.18)	4,273	40	1.60 (1.11,2.30)
p for trend			0.1			0.006
Dye color						
None	147,144	1,064	Ref	17,671	106	Ref
Light colors only	85,978	664	1.12 (1.01,1.23)	2,401	21	1.46 (0.91,2.34)
Dark colors only	74,888	529	1.04 (0.94, 1.16)	8,883	74	1.51 (1.12,2.05)
Light and dark colors	20,792	133	0.97 (0.81, 1.16)	686	3	--
Years of personal use						
None	115,391	822	Ref	13,395	94	Ref
< 5	51,631	376	1.10 (0.97,1.24)	7,427	53	1.08 (0.77,1.52)
5 or more	159,466	1,177	1.06 (0.97,1.16)	8,681	59	0.97 (0.70,1.34)
Applied to others						
No use [†]	308,822	2,265	Ref	28,087	196	Ref
Any use	21,700	137	0.94 (0.79,1.12)	2,075	12	0.88 (0.49,1.58)
<4 times per year	18,543	118	0.96 (0.80,1.16)	1,709	10	0.91 (0.48,1.74)
Every 5–8 weeks, 1+ per month	3,157	19	0.86 (0.55,1.35)	366	2	--
p for trend			0.5			
Semi-permanent dye						
Personal use in the 12 months before enrollment						
No use [†]	277,145	2,054	Ref	19,528	131	Ref
Any use	53,377	348	0.91 (0.81,1.02)	10,634	77	1.15 (0.86,1.53)
<4 times per year	32,227	218	0.97 (0.85,1.12)	6,903	47	1.10 (0.78, 1.54)
Every 5–8 weeks, 1+ per month	21,150	130	0.82 (0.69,0.98)	3,731	30	1.24 (0.83,1.84)
p for trend			0.04			0.3
Dye color						
None	277,145	2,054	Ref	19,528	130	Ref
Light colors only	18,385	127	0.94 (0.78,1.12)	929	5	0.79 (0.32,1.93)
Dark colors only	28,895	184	0.90 (0.77, 1.05)	8,590	62	1.16 (0.85,1.57)

	Non-Hispanic White			Black		
	Person-Years	Events	Adjusted HR (95% CI)	Person-Years	Events	Adjusted HR (95% CI)
Light and dark colors	3,139	15	0.69 (0.41, 1.14)	363	3	--
Years of personal use						
None	240,094	1,803	Ref	15,415	110	Ref
< 5	43,798	289	0.90 (0.80,1.02)	6,734	40	0.88 (0.61,1.27)
5 or more	40,087	271	0.88 (0.78,1.00)	6,989	48	0.99 (0.70,1.39)
Applied to others						
No use [†]	321,900	2,333	Ref	28,369	193	Ref
Any use	8,621	69	1.23 (0.96,1.56)	1,794	15	1.35 (0.79,2.29)
<4 times per year	7,534	57	1.17 (0.90, 1.52)	1,495	13	1.43 (0.81,2.53)
Every 5–8 weeks, 1+ per month	1,088	12	1.61 (0.91, 2.84)	299	2	--
p for trend			0.06			
Temporary dyes (rinses)						
Personal use in the 12 months before enrollment						
No use	312,860	2,270	Ref	21,849	148	Ref
Any use	17,662	132	1.02 (0.86,1.22)	8,314	60	1.12 (0.83,1.51)
Chemical straighteners						
Personal use in the 12 months before enrollment						
No use [†]	321,146	2,334	Ref	7,783	48	Ref
Any use	9,376	68	1.16 (0.91,1.48)	22,380	160	1.20 (0.87,1.66)
<4 times per year	5,459	37	1.09 (0.79, 1.51)	8,808	56	1.05 (0.71,1.55)
Every 5–8 weeks, 1+ per month	3,917	31	1.26 (0.88, 1.80)	13,572	104	1.30 (0.92, 1.85)
p for trend			0.2			0.1
Applied to others						
No use [†]	327,889	2,380	Ref	23,502	158	Ref
Any use	2,634	22	1.38 (0.90,2.10)	6,660	50	1.22 (0.87,1.70)
<4 times per year	2,039	19	1.55 (0.98,2.44)	4,900	38	1.27 (0.88,1.84)
Every 5–8 weeks, 1+ per month	595	3	--	1,760	12	1.08 (0.59,1.96)
p for trend						0.4

[*] models adjusted for age, education, ever oral contraceptive use (OC), parity, age at first birth, smoking status, BMI, age at menarche

Tests for interaction on the multiplicative scale: Black *permanent dye P=0.0382; Black * relaxer/straightener: p = 0.7983.

[†] For hazard ratio estimates associated with personal use in the 12 months before enrollment and application to others in the 12 months before enrollment, "No use" is the referent category for "Any use". For frequency of use, "No use" is also the referent category for "<4 times per year" and "Every 5 weeks, 1+month" and the p for trend is provided.