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Review article

A systematic review of association between use of hair products and benign and malignant gynecological conditions

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ABSTRACT

Hair products often contain chemicals like *para*-phenylenediamine (PPD) and endocrine-disrupting chemicals (EDCs); giving rise to concerns about the possible adverse effects such as hormonal disturbances and carcinogenicity. The objective of this systematic review was to evaluate the association between the use of different hair products and benign and malignant gynecological conditions. Studies were identified from three databases including PubMed, Embase, and Scopus, and evaluated in accordance with PRISMA guidelines. The risk of bias was assessed using the Newcastle-Ottawa Scale. A total of 17 English-language studies met the inclusion criteria. Associations of hair relaxer or hair dye use with breast and ovarian cancer were observed in at least one well-designed study, but these findings were not consistent across studies. Further sub-analysis showed 1.08 times (95 % CI: 1.01–1.15) increased risk of breast cancer in females with permanent hair dye use. Chang et al. reported strong association between uterine cancer risk and hair relaxer use (HR 1.8, 95 % CI: 1.12–2.88), with no observed association with hair dye use. Studies conducted by Wise et al. and James-Todd et al. for benign gynecological conditions; including uterine leiomyoma (IRR 1.17, 95 % CI: 1.06–1.30), early onset of menarche (RR 1.4, 95 % CI: 1.1–1.9), and decreased fecundability (FR 0.89, 95 % CI: 0.81–0.98) revealed positive associations with hair relaxer use, but these findings were based on small sample sizes. In summary, the available evidence regarding personal use of hair products and gynecological conditions is insufficient to determine whether a positive association exists.

Introduction

Hair is an integral component of the external covering of most mammals, responsible for creating a physical barrier between an animal and its environment [1]. In humans, although hair has no vital biological function, it has immense psychological importance for both men and women [1,2]. The appearance of hair; especially hair color, length, and style has an impact on people's overall self-perception and physical appearance [3]. Unlike most of our physical features, the appearance of our hair can be easily changed without resorting to surgical procedures [4]. Trueb et al. [5] defined hair products as, "preparations intended for placing in contact with the hair and scalp, with the purpose of cleansing, promoting attractiveness, altering appearance, and/or protecting them in order to maintain them in good condition." This broad utility of hair products is reflected in a hair cosmetic market that was valued at USD 80.81 billion in 2020 [6].

Marketing studies have associated socioculturally determined characteristics to be an important variable in consumer behavior strategies [7]. Females, when compared to males, have been found to have a greater concern for social context [8]. Hence, females are the primary targets of the hair cosmetic industry [8]. Surveys have reported that 34 % of females use hair treatments every year [9]. Additionally, racial

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differences in hair product usage have been observed which indicates African American females and children are more inclined to use hair products to meet cultural beauty standards that favor long and straight hair [10,11].

Studies have reported that hair care product use puts females at a higher risk of developing benign and malignant gynecological conditions [11–23]. It is clear that some hair care products contain chemicals such as *para*-phenylenediamine (PPD) and endocrine-disrupting chemicals (EDCs), including parabens, metals, phthalates, and formaldehyde [24–26]. These chemicals possess the ability to alter homeostasis of the endocrine system via stimulating the hypothalamic-pituitary axis leading to an increased risk of benign gynecological diseases including fibroids and early onset of menarche [27,28]. Such chemicals can also mimic the carcinogenic effects of estrogen and can disrupt the mechanism of apoptosis via the reactive oxygen pathway, increasing the risk of breast, ovarian, and uterine cancer [26]. Chemicals contained in hair products have been linked to other non-gynecological diseases as well including obesity, diabetes, lupus, bladder cancer, lung cancer, and Hodgkin's lymphoma [29,30]. Based on the prevalent use of hair products, a key question is whether their use could lead to an increased incidence of gynecological conditions. The aim of this systematic review was to evaluate available evidence pertaining to the association between different hair products and gynecological conditions, including breast and ovarian cancers.

Methods

Study design

This systematic review was conducted in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) guidelines [31].

Search strategy

Studies were identified by searching publications in PubMed, Embase, and Scopus. The data informationist designed a list of terms related to gynecological conditions and hair products including "Hair relaxers" OR "hair dyes" OR "personal care products" OR "hair straighteners" OR "perms" OR "Relaxers" AND "fibroids" OR "leiomyomata" OR "leiomyoma OR "fibromyoma" OR "myoma" OR "myomas" OR "myxomatosis" OR "uterine cancer" OR "ovarian cancer" OR "Breast Cancer" OR "Endometrial Cancer" OR "Breast Tumor" OR "Ovarian Tumor". A complete list of search strategies used is included in Appendix 1.

Inclusion and exclusion criteria

The eligibility criteria required studies to quantitatively measure gynecological conditions and at least one hair product. English-language studies on the association of the use of hair products with gynecological conditions were included. Studies were limited to human subject research and study types included case-control studies, cohort studies, and cross-sectional studies. Review articles, letters, and animal studies were excluded. The full list of eligibility criteria is listed in Appendix 2.

Study selection

After initial search strategies were performed, two independent reviewers (HF, PM) screened titles and abstracts per the eligibility criteria. Conflicts in the designation of studies inclusion were resolved by discussion, and any discrepancies were resolved by the senior authors (BS, JS). After completing the title and abstract screening, full-text screening was conducted in a similar manner using the same inclusion and exclusion criteria. Case-control studies, Cohort studies, and Cross-sectional studies that evaluated an association between Hair products and Gynecologic conditions were included in the review.

Assessment of risk of bias

Study quality and risk of bias were assessed by two reviewers independently (HF, PM) and discrepancies were resolved by the senior authors (BS, JS). The quality of studies was determined to be good, fair, or poor based on the Newcastle-Ottawa scale by the assessment of selection, comparability, and outcome sections. Studies were graded one point each for all items except comparability which had the potential to score up to two points, with the maximum possible score being nine: 1. Poor quality (0–2 points), 2. Fair quality (3–5 points) and 3. Good quality (6–9 points).

Data representation and analysis

Extracted data of studies included as per the selection criteria was categorized by the gynecologic conditions and the hair products assessed as well as the study population. Where sufficient data was available, sub-analysis of studies was performed to determine a pooled disease risk. Pooled means were calculated by the formula: "$\sum$ [(Mean of Study) x (Study Sample Size)] / $\sum$ Study Sample Size". Similarly, pooled confidence intervals were calculated using "Pooled Mean $\pm$ 1.96 x Pooled Standard Deviation" for each, where pooled standard deviations were calculated with the formula: "$\sqrt{}$ {$\sum$ [(Study Sample Size −1) (Study Standard Deviationˆ2)] / ($\sum$ Study Sample Size -Number of studies)}".

Results

The initial search yielded a total of 195 studies in Scopus, 192 studies in Embase, and 159 studies in PubMed. After duplicates were removed, 375 unique reports underwent initial title and abstract review. Thirty-two studies were considered for full-text review (Fig. 1). A total of 17 studies met the complete inclusion criteria and were included in this systematic review. These included 9 cohort studies, 6 case-control studies, and 2 cross-sectional studies. Risk of bias analysis among the 17 studies revealed 11 were of good quality, 5 were of fair quality and one was of poor quality. All studies besides Stavraky et al. [32,33] used disease risk models adjusted for age, ethnicity, and other confounding factors related to the disease. Table 1 comprehensively summarizes results of studies included in the systematic review stratified by gynecological condition and hair product studied as well as by specific study population results reported. Breast cancer was the only gynecological condition with sufficiently available data to perform a further sub-analysis to evaluate the relationship between hair product use and risk of breast cancer (Table 2).

Hair products and breast cancer

For the analysis of the association between breast cancer risk and hair products, 8 eligible studies were included. Llanos et al. [12] and Stavraky et al. [33] reported no significant association between the use of hair dyes and breast cancer risk (OR 1.1, 95 % CI: 0.95–1.32 and RR 1.5, 95 % CI: 0.7–3.1). Llanos et al. [12] used race-stratified, age-adjusted, and multi-variable adjusted (education, body mass index, family history of breast cancer, and oral contraceptive use) logistic regression models to estimate the association between breast cancer risk and hair product use. Permanent hair dye use was found to be significantly associated with breast cancer occurrence by Eberle et al. (HR 1.09, 95 % CI 1.01–1.17) [11], where they used cox proportional hazard models (with age as the time scale) adjusted for education, oral contraceptive use, parity, age at first birth, smoking status, BMI, and age at menarche. Eberle et al. [11] and Llanos et al. [12] both reported associations of breast cancer hazard risk with dark color hair dye use (HR 1.08, 95 % CI 0.98–1.19 and OR 1.51, 95 % CI 1.20–1.90 respectively)

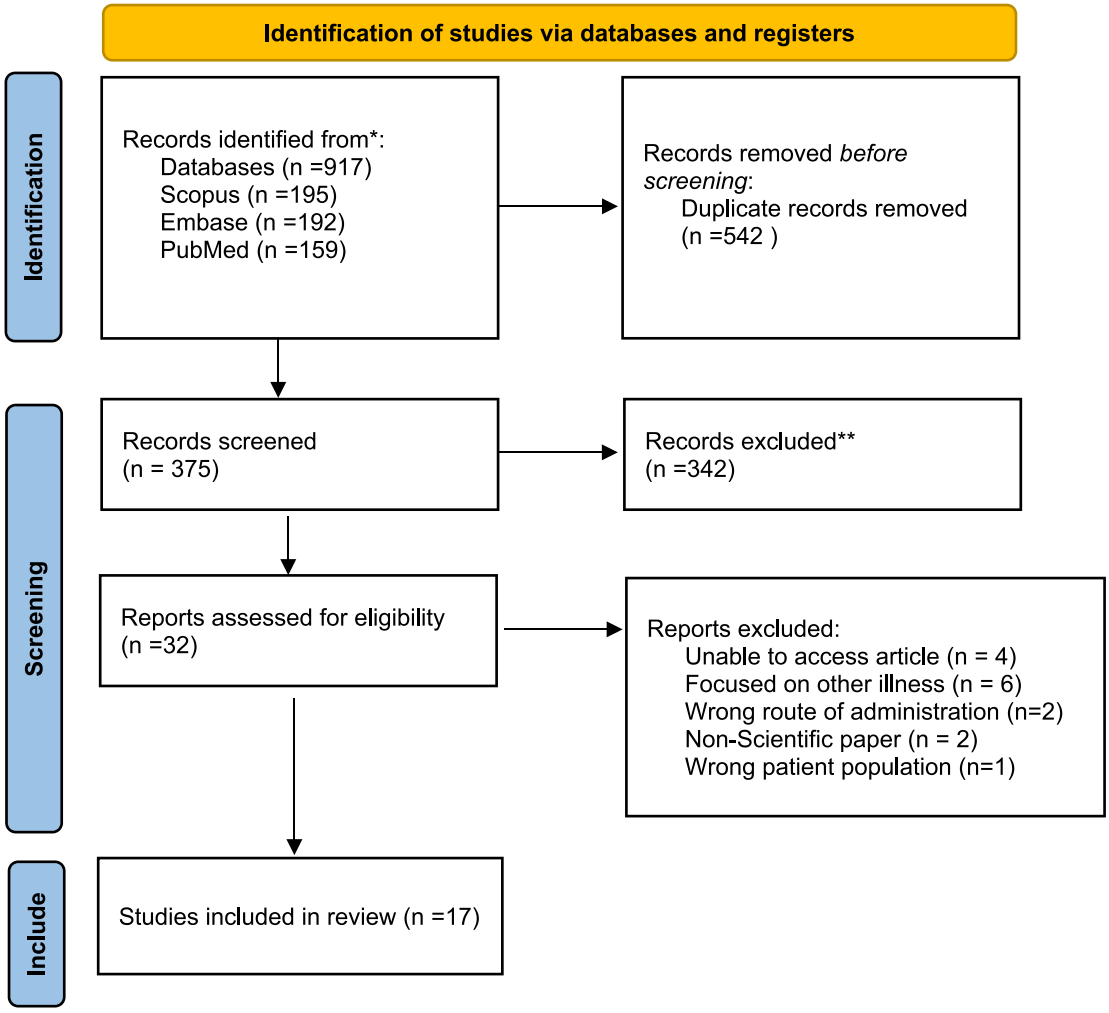

Fig. 1. PRISMA flowchart of article identification, retrieval, review and inclusion. *From:* Page MJ, McKenzie JE, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD, et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. BMJ 2021;372:n71. https://doi.org/10.1136/bmj.n71. For more information, visit: https://www.prisma-statement.org/.

and light color hair dye use (HR 1.12, 95 % CI: 1.02–1.23) [11,12]. Zhang et al. [21] reported associations of risk between permanent dark color hair dyes and ER-, PR-, ER+/PR- and ER-/PR- breast cancer (HR = 1.16, 95 % CI: 0.98–1.37) (HR = 1.13, 95 % CI: 0.99–1.29) (HR = 1.11, 95 % CI: 0.92–1.35) (HR = 1.15, 95 % CI = 0.96–1.38) (HR = 1.21, 95 % CI: 1.00–1.47); by controlling confounding factors using a cox proportional hazard regression model adjusted for age, race, natural hair color, body mass index, smoking status, pack years of smoking, and alcohol intake. For hair relaxer use, no impact on overall relation with breast cancer risk was reported by Llanos et al. [12] and Coogan et al. [13] in a sample size of 54,828 females; based on frequency > 4 times/year (HR = 1.30, 0.92–1.85 and HR = 0.99, 0.86–1.15) and duration > 10 years (HR = 1.04, 0.88–1.22). Coogan et al. [13] analyzed breast cancer risk using cox proportional hazards regression models adjusted for age, region, oral contraceptive use, body mass index, age at menarche, and number of mammograms received up to 4 years prior to breast cancer diagnoses. Eberle et al. [11] reported a positive association of breast cancer risk with hair relaxer use (HR = 1.18, 95 % CI 0.99–1.41) and increased frequency > 4 times/year (p for trend = 0.02) among 46,709 participants from the Sister Study sample. Further sub-analysis in Table 2 showed an increased risk of breast cancer in females with permanent hair dye use (mean disease risk reported:1.08, 95 % CI 1.01–1.15). No other conclusive statement could be made for any other hair product.

Hair products and uterine cancer

Studies conducted by Stavraky et al. [32,33] reported no association between hair dye use and uterine cancer incidence (RR = 1.6, 95 % CI 0.6–4.0, and RR = 1.3, 95 % CI 0.5–3.1 respectively). Chang et al. [15] and Stavraky et al. [32] also reported no association between uterine cancer risk and the type of hair dye used: permanent (HR = 0.90, 0.74–1.11 and HR = 1.1, 0.5–2.3) and semi-permanent dye (HR = 0.94, 95 % CI 0.72–1.24 and HR = 1.4, 95 % CI 0.5–3.6). Chang et al. [15] used cox models adjusted for race, educational attainment, body mass index, physical activity, menopausal status at enrollment, parity, smoking status, alcohol consumption, oral contraceptive use duration, hormone replacement therapy, and age at menarche. Hair relaxer use was found to be significantly associated with uterine cancer risk with a reported HR value of 1.8 (95 % CI = 1.12–2.88) as well as a HR of 2.55 (95 % CI = 1.46–4.45 at p(trend) = 0.002) linked with increased frequency of use [15]. The observed high rates of uterine cancer occurrence and hair relaxer use were reported in pre-menopausal (HR 1.56, 95 % CI = 0.26 to 9.29) and post-menopausal women (HR 2.52, 95 % CI = 1.39 to 4.55) at p = 0.003. Hair relaxer use was also associated with type 1 endometrial cancer risk (frequent use: HR = 2.94, 95 % CI = 1.42 to 6.08) [15].

Table 1
Summary of Studies Evaluating the Demographic Relationship between Hair Product Use and Risk of Gynecological Condition.

References	Study Design	Sample Size	Study Location	Exposure Assessment Tool	Gynecological Condition Evaluated	Hair Product Use	Study Population (events)	Disease Risk Reported*			Risk Of Bias Analysis (In Accordance with Newcastle Ottawa Scale)
								History of Use	Increased Duration of Use	Increased Frequency of Use	
Llanos AAM et al (2017)	Case-control study	N = 4,285 Age 20–75 years	USA (NYC)	In-person interviews	Breast Cancer	Hair dye	Non-white (1508)	1.12 (0.95, 1.32)	1.03 (0.81, 1.31)	1.20 (0.93, 1.54)	Good
							White (772)	1.07 (0.86, 1.32)	1.03 (0.80, 1.33)	0.99 (0.77, 1.28)	
						Hair relaxer	Non-white (1508)	0.99 (0.79, 1.26)	1.07 (0.80, 1.43)	0.93 (0.73, 1.19)	
							White (772)	**1.74 (1.11, 2.74)**	1.18 (0.16, 8.82)	**3.15 (1.57, 6.31)**	
						Deep conditioning cream	Non-white (1508)	0.92 (0.78, 1.08)	x	x	
							White (772)	1.30 (0.85, 1.99)	x	x	
Eberle CE et al (2019)	Prospective cohort	N = 46,709 Age 35–74 years	USA (Puerto Rico)	Computer-assisted telephone interviews	Breast Cancer	permanent hair dye	Females (2794)	1.09 (1.01, 1.17)	1.05 (0.96, 1.14)	1.09 (1.00, 1.19)	Good
							Non-white (208)	**1.45 (1.10,1.90)**	0.97 (0.70,1.34)	**1.60 (1.11,2.30)**	
							White (2402)	1.07 (0.99,1.16)	1.06 (0.97,1.16)	1.08 (0.98,1.18)	
						semi-permanent hair dye	Females (2794)	0.96 (0.87, 1.06)	0.90 (0.80,1.00)	0.91 (0.78, 1.06)	
							Non-white (208)	1.15 (0.86,1.53)	0.97 (0.70,1.34)	1.24 (0.83,1.84)	
							White (2402)	0.91 (0.81,1.02)	1.06 (0.97,1.16)	**0.82 (0.69,0.98)**	
						Hair relaxer	Females (2794)	**1.18 (0.99,1.41)**	x	**1.31 (1.05,1.63)**	
							Non-white (208)	1.20 (0.87,1.66)	x	1.30 (0.92, 1.85)	
							White (2402)	1.16 (0.91,1.48)	x	1.26 (0.88, 1.80)	
Coogan PF et al (2021)	Prospective cohort	N = 50,543 Age 21–69 years	USA	Self-administered questionnaire	Breast Cancer	Hair relaxer	Females (2311)	1.05 (0.9, 1.20)	1.02 (0.89,1.18)	1.12 (0.94,1.34)	Good
Rao R et al (2021)	Case-control study	N = 2,998 women, Age 20–75 years	USA (NYC and NJ)	In-person home and computer-assisted interviews	Breast Cancer-Tumor grade (Moderately differentiated)	Hair relaxer	Females (2998)	1.04 (0.81, 1.34)	1.26 (0.73, 2.15)	x	Good
							Non-white (2227)	1.02 (0.75, 1.40)	1.29 (0.78, 2.13)	x	
							White (771)	1.02 (0.66, 1.59)	1.26 (0.73, 2.15)	x	
					Breast Cancer-Tumor grade (Poorly differentiated)		Females (2998)	1.07 (0.82, 1.38)	1.23 (0.69, 2.19)	x	
							Non-white (2227)	1.03 (0.76–1.41)	1.58 (0.95–2.62)	x	
							White (771)	1.11 (0.68–1.77)	1.23 (0.69–2.19)	x	
Taylor KW et al (2018)	Prospective cohort	N = 46,905 Age 35–74 years	USA (Puerto Rico)	Computer-assisted interviews and self-administered questionnaire	Breast Cancer	Hair relaxer	Non-white (180)	0.90 (0.63, 1.28)	x	x	Good
							White (2146)	0.91 (0.70, 1.19)	x	x	

(*continued on next page*)

Table 1 (*continued*)

References	Study Design	Sample Size	Study Location	Exposure Assessment Tool	Gynecological Condition Evaluated	Hair Product Use	Study Population (events)	Disease Risk Reported*			Risk Of Bias Analysis (In Accordance with Newcastle Ottawa Scale)
								History of Use	Increased Duration of Use	Increased Frequency of Use	
					Breast Cancer-Post menopausal		White (1454)	0.76 (0.71, 0.81)	x	x	
Zhang Y et al (2020)	Prospective cohort	N = 11,7200 Age 30–55 years	USA	Self-administered questionnaire	Breast Cancer	permanent hair dye	Females (9252)	1.02 (0.98, 1.07)	x	1.09 (1.02, 1.16)	Good
					Ovarian Cancer		Females (1215)	1.09 (0.97, 1.22)	x	1.15 (0.96, 1.37)	
Stavraky KM et al (1979)	Case-control	N = 1179 women	UK, Canada	Self-administered questionnaire	Breast Cancer (Toronto)	Hair dye	White (21)	1.5 (0.7, 3.1)	x	x	Fair
					Breast Cancer (London)		White (36)	0.7 (0.3,1.7)	x	x	
					Uterine Cancer		White (28)	1.3 (0.5,3.1)	x	x	
					Breast Cancer (Toronto)	permanent hair dye	White (16)	1.3 (0.6, 2.5)	x	x	
					Breast Cancer (London)		White (28)	1.1 (0.5, 2.4)	x	x	
					Uterine Cancer		White (19)	1.1 (0.5, 2.3)	x	x	
					Breast Cancer (Toronto)	semi-permanent hair dye	White (2)	1.7 (0.4, 6.5)	x	x	
					Breast Cancer (London)		White (4)	0.3 (0.1, 1.7)	x	x	
					Uterine Cancer		White (9)	1.4 (0.5, 3.6)	x	x	
Stavraky KM et al (1981)	Case-control	N = 537 women	UK, Canada	Self-administered questionnaire	Breast (Toronto)	Hair dye	Females (35)	1.1 (0.5, 2.7)	x	x	Fair
					Breast (London)		Females (50)	1.2 (0.6, 2.6)	x	x	
					Uterine (Toronto)		Females (36)	1.6 (0.6, 4.0)	x	x	
					Ovarian Cancer (Toronto)		Females (41)	1.6 (0.6, 4.8)	x	x	
					Ovarian Cancer (London)		Females (17)	0.2 (0.02, 1.2)	x	x	
Chang CJ et al (2022)	Prospective cohort study	N = 33,947 Age 35–74 years	USA (Puerto Rico)	Self-administered questionnaire	Uterine Cancer	permanent hair dye	Females (185)	0.90 (0.74, 1.11)	0.82 (0.64, 1.05)	0.98 (0.78, 1.24)	Good
						semi-permanent hair dye	Females (64)	0.94 (0.72, 1.24)	0.98 (0.67, 1.44)	0.90 (0.60, 1.35)	
						Hair relaxer	Females (38)	**1.80 (1.12, 2.88)**	x	**2.55 (1.46, 4.45)**	
							Non-white (23)	1.66 (0.67, 4.09)	x	2.12 (0.83, 5.39)	
							White (12)	**1.94 (1.09, 3.47)**	x	**2.66 (1.25, 5.67)**	
Hennekens CH et al (1979)	Cross-sectional study	N = 12,0557 Age 30–55 years	USA	Self-administered questionnaire	Cervical Cancer	permanent hair dye	Females (571)	1.44	x	x	Poor
					Vagina Cancer		Females (90)	2.58	x	x	
Tzonou A et al (1993)	Case-control study	N = 389 women Age < 75 years	Athens	In-person interviews	Ovarian Cancer	Hair dye	Females (77)	x	x	**2.16 (1.19, 3.89)**	Fair

(*continued on next page*)

Table 1 (*continued*)

References	Study Design	Sample Size	Study Location	Exposure Assessment Tool	Gynecological Condition Evaluated	Hair Product Use	Study Population (events)	Disease Risk Reported*			Risk Of Bias Analysis (In Accordance with Newcastle Ottawa Scale)
								History of Use	Increased Duration of Use	Increased Frequency of Use	
White AJ et al (2021)	Prospective cohort	N = 40,559 Age 35–74 years	USA	Self-administered questionnaire	Ovarian Cancer	permanent hair dye	Females (130)	1.07 (0.82, 1.39)	1.06 (0.78, 1.43)		Good
							Non-white (7)	0.63 (0.25, 1.55)	x	0.92 (0.30, 2.85)	
							White (116)	1.14 (0.86, 1.52)	x	1.14 (0.83, 1.57)	
						semi-permanent hair dye	Females (50)	1.17 (0.85, 1.60)	1.17 (0.76, 1.82)	1.33 (0.87, 2.04)	
							Non-white (11)	2.05 (0.86, 4.88)	x	**3.06 (1.08, 8.63)**	
							White (35)	1.02 (0.71, 1.47)	x	1.10 (0.66, 1.83)	
						Hair relaxer	Females (24)	1.29 (0.70, 2.38)	x	**2.19 (1.12, 4.27)**	
							Non-white (17)	1.28 (0.46, 3.52)	x	1.82 (0.64, 5.18)	
							White (4)	0.89 (0.33, 2.40)	x	1.55 (0.49, 4.86)	
James Todd T et al (2011)	Cross-sectional study	N = 300 Age 18–77 years	USA (NYC)	In-person interviews	Early Menarche	Hair relaxer	Females (50)	**1.4 (1.1, 1.8)**	x	x	Fair
						Deep conditioning cream	Females (45)	1.3 (1.0, 1.6)	x	x	
						Hair Oil	Females (165)	**1.4 (1.1, 1.9)**	x	x	
Mcdonald JA et al (2018)	Cohort study	N = 248 Age 40–60 years	USA (NYC)	Self-administered questionnaire	Early Menarche	Hair Oil	Females (148)	2.32 (0.98, 5.48)	x	x	Fair
Wise LA et al (2023)	Cohort study	N = 11,274 Age 21–45 years	USA and Canada	Self-administered questionnaire	Fecundability	Hair relaxer	Females (1133)	**0.89 (0.81, 0.98)**	**0.71 (0.54, 0.91)**	0.82 (0.60, 1.11)	Good
Wise LA et al (2012)	Cohort study	N = 59,000 Age 21–69 years	USA	Self-administered questionnaire	Uterine Leiomyomata	Hair relaxer	Non-white (6766)	**1.17 (1.06, 1.30)**	**1.20 (1.07, 1.34)**	**1.23 (1.10, 1.37)**	Good
Peinado F.M. et al (2021)	Case-control study	N = 124 Age 20–54 years	Spain	Urinary samples and self-administered questionnaires	Endometriosis	Hair dye	Females (35)	x	x	x	Good

*Bold results are reported to be statistically significant

Table 2
Sub-analysis of Studies Evaluating the Relationship Between Hair Product Use and Risk of Breast Cancer, by Race.

Gynecological Disease	History of Hair Product Use	Study Population	Mean Disease Risk Reported	95 % Confidence Interval	Studies Included
Breast Cancer	Hair Relaxer	All Female	1.13	0.85–1.40	[11,13,22]
		White	1.07	0.74–1.39	[10,11,12,22]
		Non-white	1.05	0.69–1.4	[10,11,12,22]
	Hair Dye	All Female	1.15	0.10–2.20	[12,32]
		White	1.08	0.53–1.62	[12,33]
		Non-white	_	_	
	Permanent Hair Dye	All Female	1.08	1.01–1.15	[11,21]
		White	1.07	0.88–1.26	[11,33]
		Non-white	_	_	
	Semi-permanent Hair Dye	All Female	_	_	
		White	0.92	0.50–1.33	[11,33]
		Non-white	_	_	

Hair products and ovarian cancer

Tzonou et al. [19] and Stavraky et al. [32] reported significant associations between hair dyeing and ovarian cancer risk with reported RR of 2.16 (95 % CI = 1.19–3.89) and 1.60 (95 % CI = 0.6–4.8) among 1,040 females. Tzonou et al. [19] used multivariate analysis controlled for age, years of schooling, weight before onset of the disease, age at menarche, menopausal status, parity, age at first birth, tobacco smoking, average consumption of alcoholic beverages and average coffee drinking. White et al. [20] reported no significant association with either permanent HR = 1.07 (95 %CI = 0.82–1.39) or semi-permanent hair dye = HR 1.17 (95 % CI = 0.85–1.60) in 50,884 study participants, but a possible association between frequent hair dye use > 4 times/year and ovarian cancer risk (HR = 1.33, 95 % CI 0.82–1.45); by using cox proportional hazard regression (with time-scale as age) adjusted for race, education, BMI, age at menarche, menopausal status, parity, oral contraceptive use, hormone therapy uses, hysterectomy status, tubal ligation status, smoking, and alcohol use. In the investigation of hair product effect on different types of ovarian cancer, the use of permanent hair dye was positively associated with non-serous ovarian cancer (HR 1.94, 95 % CI:1.12–3.37) but inversely associated with serous tumors (HR = 0.65, 95 % CI0.43–0.99)[20]. Ovarian cancer risk was also found to be positively associated with the use of hair relaxer HR value of 1.29 (95 % CI = 0.70–2.38) and increased frequency of its use (HR 2.19, 95 % CI = 1.12–4.27, p for trend = 0.03) [20].

Hair products and cervical cancer

Hennekens et al. [34] found a significant association between permanent hair dye use and cervical cancer risk (RR = 1.44, P < 0.001) in a sample size of 120,557. This value remained statistically significant even after making adjustments for cigarette smoking (chi-square reduced from 13.48 to 8.26) [34]. Stavraky et al. [32] reported no significant association between the use of hair dye and cervical cancer (RR = 0.7, 95 % CI: 0.3–1.9) among 786 females.

Hair products and early menarche

Childhood hair oil use was strongly associated with the onset of early menarche (<12 years) among 548 females as reported by James Todd et al. [35] and McDonald et al. [23] (RR = 1.4, 95 % CI 1.1–1.9) (RR = 2.32, 95 % CI 0.98–5.48); where they both used disease risk ratios adjusted for age and race. Women who initiated hair oil use at least 2 years before menarche reported a positive association with younger age at menarche RR = 5.3 (95 % CI: 1.5–19.1) [14]. Childhood perms/ relaxers use was linked with early onset of menarche (RR = 1.4, 95 % CI:1.1–1.8). Hair lotions and leave-in conditioners were not associated with early onset of menarche (RR = 1.1, 95 % CI: 0.8–1.4 and RR = 1.3, 95 % CI: 1.0–1.6) [23].

Hair products and fecundability

The use of hair relaxers at least once, in both current and former users was associated with lower fecundability (FR = 0.81, 95 % CI: 0.64, 1.03) (FR = 0.89, 95 % CI: 0.81, 0.98) as reported by Wise et al. [18]; where they used fecundability ratios adjusted for age, education, race, annual household income, BMI, smoking status, marital status, relationship duration, parity last method of contraception, intercourse frequency, and history of perm. FRs for the first use of hair relaxers at ages < 10, 10–19, and ≥ 20 years were reported as 0.73 (95 % CI: 0.55, 0.96), 0.93 (95 % CI: 0.83, 1.04), and 0.85 (95 % CI: 0.74, 0.98) respectively. Fecundability was reported as lowest among those with longer durations of use (≥10 years vs. never: FR = 0.71, 95 % CI: 0.54–0.91) and more frequent use (≥5 times/year vs. never: FR = 0.82, 95 % CI: 0.60–1.11), but associations were nonmonotonic [18].

Hair products and fibroids (Uterine Leiomyoma)

Wise et al. [17] found a positive association between the use of hair relaxers and fibroid risk among 59 000 females (IRR = 1.17, 95 % confidence interval: 1.06–1.30); by constructing a multi-variable model that adjusted for age, time period, age at menarche, parity, age at first birth, years since last birth, oral contraceptive use, body mass index, smoking alcohol use, education marital status, occupation, household income, and country of birth. An overall correlation was found between fibroid risk and hair relaxer use based on number of burns (P trend < 0.001), duration of use (P trend = 0.015), and frequency of use (P trend < 0.001). Strong associations were observed based on the increased frequency of use for leaner women (p trend = 0.003) and women living in the South region (p trend = 0.004) of the USA, but there was no evidence of statistical interaction by body mass index or region. No risk for fibroids was related to age at first use (P trend = 0.27) or type of formulation: lye (IRR:1.21, 95 % CI: 1.08–1.36) vs no lye (IRR: 1.18, 95 % CI: 1.06–1.31) [17].

Hair products and endometriosis

Peinado et al. [16] reported an association between the use of hair dye and high levels of urinary EtP, PrP, and BP-1 among 124 participants (expB = 2.50, 95 % CI: 0.02–1.81, p-value: 0.045), (expB = 3.60, 95 % CI: 0.40–2.16, p-value: 0.00) and (expB = 2.28, 95 % CI:0.04–1.60, p-value: 0.039); where they used regression analyses adjusted for urinary creatinine, age, BMI, parity, and residence. Benzophenones and parabens, specifically BP-1, BP-3, and Parabens MeP were associated with a higher risk of endometriosis (OR = 5.12, 95 % CI: 1.46–17.99), (OR = 4.98, 95 % CI: 1.52–16.31) and (OR = 3.34, 95 % CI: 1.11–10.05). EtP was found to have no significant effect on endometriosis (OR = 0.98, 95 % CI: 0.33–2.91) [16].

Discussion

Sister Study participants were evaluated by Eberle et al. [11], White et al. [20], Chang et al. [15], and Wise et al. [17] for the association between hair relaxer association and breast, ovarian, uterine cancer, and uterine leiomyoma respectively. Eberle et al. [11] found an 18 % higher breast cancer risk with the use of hair relaxers. Similarly, White et al. [20] reported a significant and dose-dependent positive trend indicating a two-fold increase in the risk of ovarian cancer. Chang et al. [15] reported negligible associations between hair relaxer use with uterine cancer risk. Benign gynecological conditions including fecundability and uterine leiomyoma were also found to be significantly associated with the use of hair relaxers, frequency, and duration [17,18]. Positive associations were also observed between the total number of burns experienced during hair relaxer use and the risk of uterine leiomyoma [17].

One reason for the positive association is that these hair relaxers have been found to release endocrine-disrupting compounds (EDCs), including parabens, metals, phthalates, and formaldehyde [24,25,36]. EDCs can potentially mimic the actions of estrogen and interfere with estrogen and non-estrogen-dependent pathways to promote the growth of malignancies [37]. Animal studies have found different mechanisms linking breast cancer risk with EDC exposure, including changes in fetal mammary gland development that increase sensitivity to carcinogenesis [38]. Even though ovarian cancer is not an estrogen-dependent tumor, studies conducted in vitro have found EDC-stimulated proliferation of ER-positive BG-1 ovarian cancer cells [39]. EDCs are known to alter the homeostasis of the endocrine system by stimulating the hypothalamic-pituitary–gonadal axis and increasing the secretion of gonadotropins and hence ovarian steroids [28]. PCOS has been associated with unopposed estrogen exposure, but no study has evaluated the relationship between PCOS and hair product use. Similarly, uterine leiomyoma development has also been linked to increased levels of unopposed estrogen [40]. Phthalates are endocrine-disrupting chemicals and their role in uterine leiomyoma development has been studied by the Third National Health and Nutrition Examination Survey (NHANES), which showed positive and inverse associations with mono butyl phthalate and mono(2-ethylhexyl) phthalate [41]. While there is limited human data linking EDCs to the early onset of menarche, data from animal models have provided more evidence supporting this association [42]. Early exposure to EDCs in female rats has been found to influence infantile female hypothalamic pituitary maturation through the early developmental acceleration of GnRH secretion and subsequently sexual precocity [27].

Studies related to hair dye use found permanent and dark color hair dye usage to be particularly associated with breast cancer risk, similar to the results of our sub-analysis table. On the contrary, no significant association was found between ovarian and uterine cancer risk with these particular hair dye types by Tzonou et al. [19] and Stavraky et al. [32] in the years 1993 and 1981 respectively. However, White et al. [20] in the year 2021 reported a positive association between increased frequency of hair dye use and ovarian cancer occurrence. One possible explanation for differences in these results is the change in product formulations of hair dyes over time; oxidative hair dyes were introduced in the market at the end of the 19th century and have since then experienced explosive growth in consumption [43]. Among benign gynecological conditions, only endometriosis risk has been studied and associated with personal use of hair dyes [16]. Previous studies have linked the use of permanent hair dyes with an increased risk of Hodgkin lymphoma, bladder cancer, lung cancer, and SLE [29,44].

Hair dyes contain PPD (*para*-phenylenediamine) as their main precursor, which can promote the growth of cancer. PPD works by activating the reactive oxygen species-mediated mitochondrial pathway and inhibits the mTOR, NF-kB, and Wnt pathways; disrupting the mechanism of apoptosis [26]. Animal studies have found PPD-associated oxidative DNA damage in breast cancer [45]. Hair dye use has also been associated with increased levels of parabens and benzophenones in the human body. These chemicals have been found to increase the risk of endometriosis through an oxidative stress-independent manner [16].

Our study provides a summary of the research gaps in the literature around hair product use and gynecological conditions. All of the significant findings related to benign gynecological conditions should be approached with caution because they are based on a small study sample size and are subject to recall bias due to population surveys. Further studies are needed to investigate the relationship between ovarian cancer, and benign gynecological conditions with hair dyes, and hair relaxers. Similarly, little is known about the underlying mechanism linking ovarian cancer and benign gynecological diseases to hair products and needs further research. To comprehensively evaluate exposure assessment, studies of hair products should include at a minimum information on the duration, frequency, type of product (hair dye-permanent/ semi-permanent, hair relaxer-lye/ no-lye), and color (hair dye-dark/light). Furthermore, they should determine the extent of potential confounding by adjusting disease risk ratios for at least age, ethnicity, and exposure assessment.

FDA is responsible for managing the safety of hair products sold in the US and can ban any product found harmful, except for coal-tar-containing hair dyes [46]. Nowadays, most hair dye products contain ingredients derived from petroleum sources but have been considered coal-tar dyes by the FDA. According to the Scientific Committee on Consumer Safety (SCCS), permanent hair dyes are considered safe for use below a certain limit of concentrations but have noticed inconsistent results regarding genotoxicity, and need further explanation in epidemiological studies [47]. Therefore, a regulatory risk assessment should potentially expand to cover all hair care products, including coal-tar hair dyes, hair relaxers, and hair oils.

This review is strengthened by the broad eligibility criteria. In addition, it included up-to-date studies related to hair products and associated gynecological conditions. The majority of these studies controlled confounding factors in statistical analysis, including age and ethnicity for both benign and malignant conditions. Admittedly, this review has some limitations. First, only English publications were included in our study, which might lead to selection bias. Second, we used all studies for the review regardless of the risk of bias due to the limited number of studies. Third, we only had a small number of identified publications investigating benign gynecological (early menarche, fibroids, endometriosis, and fecundability) and malignant conditions (ovarian and uterine cancers) compared to breast cancer publications, which might lead to result bias. Fourth, we were not able to assess the formulation of the hair dyes or relaxers used in different studies as they were not reported. Fifth, differences in study design, population and chemical formulations used might cause clinical heterogenicity. Lastly, a limitation for our study is the variance in cutoff for early menarche in studies determining association of onset of menarche with hair product use prior to the menarche. While we used authors' [23,35] cut-offs of onset less than 12 years, it's worth noting that there is no standard guideline for cut-off age to define early menarche by associations. This may impact the generalizability of our findings and should be considered when interpreting the results.

Conclusion

The available evidence regarding personal hair product use and gynecological conditions is insufficient to conclude whether a positive association exists. To further evaluate the role of hair product use in benign and malignant gynecological conditions, comprehensive exposure assessment and risk analysis are needed.

Authors' contributions:

All authors contributed to the design of the study, execution of the study and/or drafting of the publication and all authors confirm the

validity of the results.

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Ethics approval and consent to participate

Not applicable.

CRediT authorship contribution statement

Hajra Farooq: Data curation, Investigation, Writing – original draft, Writing – review & editing. **Pauras Mhatre:** Data curation, Formal analysis, Visualization, Writing – original draft, Writing – review & editing. **Riya Aggarwal:** Data curation, Methodology, Writing – original draft. **Mahalia T. Robinson:** Conceptualization, Data curation, Writing – original draft. **Emily Joseph:** Data curation, Resources. **James Segars:** Conceptualization, Investigation, Methodology, Supervision, Validation, Writing – original draft, Writing – review & editing. **Bhuchitra Singh:** Conceptualization, Formal analysis, Investigation, Methodology, Project administration, Supervision, Validation, Writing – original draft, Writing – review & editing.

Declaration of competing interest

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.

Acknowledgments

None.

Code availability

N/A

Appendix 1. . Search terms by database and concepts

Data Base	Concept	Search Statements
Embase	Association of use of Hair Products and various benign and Malignant Gynecological conditions.	('cosmetic'/exp OR 'cosmetic' OR 'phthalic acid'/exp OR 'phthalic acid' OR 'hair lotion'/exp OR 'hair lotion' OR 'octyl dimethyl 4 aminobenzoic acid'/exp OR 'octyl dimethyl 4 aminobenzoic acid' OR '4 methoxycinnamic acid 2 ethylhexyl ester'/exp OR '4 methoxycinnamic acid 2 ethylhexyl ester' OR 'benzophenone 2′/exp OR 'benzophenone 2′ OR 'benzophenone 1′/exp OR 'benzophenone 1′ OR 'benzophenone'/exp OR 'benzophenone' OR 'glycol ether'/exp OR 'glycol ether' OR 'diethylene glycol monomethyl ether'/exp OR 'diethylene glycol monomethyl ether' OR 'diethylene glycol monoethyl ether'/exp OR 'diethylene glycol monoethyl ether' OR '2 phenoxyethanol'/exp OR '2 phenoxyethanol' OR '2 butoxyethanol'/exp OR '2 butoxyethanol' OR 'alkylphenol'/exp OR 'alkylphenol' OR 'nonylphenol diethoxylate'/exp OR 'nonylphenol diethoxylate' OR 'nonylphenol monoethoxylate'/exp OR 'nonylphenol monoethoxylate' OR '4 nonylphenol'/exp OR '4 nonylphenol' OR '4 tert octylphenol'/exp OR '4 tert octylphenol' OR '4 octylphenol'/exp OR '4 octylphenol' OR 'ethanolamine derivative'/exp OR 'ethanolamine derivative' OR 'triclosan'/exp OR 'triclosan' OR '4,4 isopropylidenediphenol' OR 'phthalic acid dioctyl ester'/exp OR 'phthalic acid dioctyl ester' OR 'di isononyl phthalate'/exp OR 'di isononyl phthalate' OR 'di isobutyl phthalate'/exp OR 'di isobutyl phthalate' OR 'phthalic acid benzyl butyl ester'/exp OR 'phthalic acid benzyl butyl ester' OR 'bis 2 ethylhexyl adipate'/exp OR 'bis 2 ethylhexyl adipate' OR 'monobutyl phthalate'/exp OR 'monobutyl phthalate' OR 'phthalic acid 2 ethylhexyl monoester'/exp OR 'phthalic acid 2 ethylhexyl monoester' OR 'monoethylhexyl phthalate'/exp OR 'monoethylhexyl phthalate' OR '4 hydroxybenzoic acid ester'/exp OR '4 hydroxybenzoic acid ester' OR 'butyl paraben'/exp OR 'butyl paraben' OR 'ethyl paraben'/exp OR 'ethyl paraben' OR 'methyl paraben'/exp OR 'methyl paraben' OR 'nonylphenol'/exp OR 'nonylphenol' OR 'fragrance'/exp OR 'fragrance' OR 'phthalic acid diethyl ester'/exp OR 'phthalic acid diethyl ester' OR 'phenethyl alcohol'/exp OR 'phenethyl alcohol' OR 'musk xylene'/exp OR 'musk xylene' OR 'musk ketone'/exp OR 'musk ketone' OR 'isobornyl acetate'/exp OR 'isobornyl acetate' OR '1 3 4 6 7 8 hexahydro 4 6 6 7 8 8 hexamethylcyclopenta g 2 benzopyran'/exp OR '1 3 4 6 7 8 hexahydro 4 6 6 7 8 8 hexamethylcyclopenta g 2 benzopyran' OR 'diphenyl ether'/exp OR 'diphenyl ether' OR 'terpineol'/exp OR 'terpineol' OR 'pinene'/exp OR 'pinene' OR 'salicylic acid methyl ester'/exp OR 'salicylic acid methyl ester' OR 'methyl eugenol'/exp OR 'methyl eugenol' OR 'linalool'/exp OR 'linalool' OR 'limonene'/exp OR 'limonene' OR 'eugenol'/exp OR 'eugenol' OR 'oxybenzone'/exp OR 'oxybenzone' OR 'octamethylcyclotetrasiloxane'/exp OR 'octamethylcyclotetrasiloxane' OR 'decamethylcyclopentasiloxane'/exp OR 'decamethylcyclopentasiloxane' OR 'phthalic acid bis(2 ethylhexyl) ester'/exp OR 'phthalic acid bis(2 ethylhexyl) ester' OR 'dpp'/exp OR 'dpp' OR 'dichloromethane'/exp OR 'dichloromethane' OR 'formaldehyde'/exp OR 'formaldehyde' OR 'sodium hydroxide'/exp OR 'sodium hydroxide' OR 'calcium hydroxide'/exp OR 'calcium hydroxide' OR 'thioglycolic acid'/exp OR 'thioglycolic acid' OR 'diethylstilbestrol'/exp OR 'diethylstilbestrol' OR 'polychlorinated biphenyl'/exp OR 'polychlorinated biphenyl' OR 'dioxin'/exp OR 'dioxin' OR 'ultraviolet filter'/exp OR 'ultraviolet filter' OR 'glycol ether derivative'/exp OR 'glycol ether derivative' OR 'alkylphenol polyoxyethyl ether'/exp OR 'alkylphenol polyoxyethyl ether' OR 'alkylphenol derivative'/exp OR 'alkylphenol derivative' AND 'lotion*':ti,ab,kw OR 'relaxer*':ti,ab,kw OR 'straightener*':ti,ab,kw OR 'octyl dimethyl':ti,ab,kw OR 'octinoxate':ti,ab,kw OR 'benzophenone-2′:ti,ab,kw OR 'benzophenone-1′:ti,ab,kw OR 'benzophenone':ti,ab,kw OR 'cyclosiloxanes':ti,ab,kw OR 'glycol ether*':ti,ab,kw OR '2,2-butoxyethoxyethanol':ti,ab,kw OR '2,2-ethoxyethoxyethanol':ti,ab,kw OR '2,2-methoxyethoxyethanol':ti,ab,kw OR '2-benzyloxyethanol':ti,ab,kw OR '2-phenoxyethanol':ti,ab,kw OR '2-butoxyethanol':ti,ab,kw OR 'alkylphenol':ti,ab,kw OR 'nonylphenol diethoxylate':ti,ab,kw OR 'nonylphenol monoethoxylate':ti,ab,kw OR '4-t-nonylphenol':ti,ab,kw OR 'octylphenol diethoxylate':ti,ab,kw OR 'octylphenol monoethoxylate':ti,ab,kw OR '4-t-octylphenol 6′:ti,ab,kw OR 'ethanolamines':ti,ab,kw OR 'ethanolamine':ti,ab,kw OR 'diethanolamine':ti,ab,kw OR 'monoethanolamine':ti,ab,kw OR 'triclosan':ti,ab,kw OR 'o-phenylphenol':ti,ab,kw OR 'bisphenol a':ti,ab,kw OR 'bpa':ti,ab,kw OR 'bpas':ti,ab,kw OR 'phthalates':ti,ab,kw OR 's-7 di-n-octyl phthalate':ti,ab,kw OR 'di-n-hexyl phthalate':ti,ab,kw OR 'di-n-

(*continued on next page*)

(*continued*)

Data Base	Concept	Search Statements
		butylphthalate':ti,ab,kw OR 'di-isononyl phthalate':ti,ab,kw OR 'di-isobutyl phthalate':ti,ab,kw OR 'di-cyclohexyl phthalate':ti,ab,kw OR 'benzylbutyl phthalate':ti,ab,kw OR 'bis(2-ethylhexyl) adipate':ti,ab,kw OR 'monobutyl phthalate':ti,ab,kw OR 'mono(2-ethylhexyl) phthalate':ti,ab,kw OR 'monoethylhexyl phthalate':ti,ab,kw OR 'parabens':ti,ab,kw OR 'butyl paraben':ti,ab,kw OR 'ethyl paraben':ti,ab,kw OR 'methyl paraben':ti,ab,kw OR 'nonylphenols':ti,ab,kw OR 'asthma associated chemical*':ti,ab,kw OR 'fragrance*':ti,ab,kw OR 'perfume*':ti,ab,kw OR 'diethyl phthalate':ti,ab,kw OR 'dep':ti,ab,kw OR 'phenethyl alcohol':ti,ab,kw OR 'musk xylene':ti,ab,kw OR 'musk ketone':ti,ab,kw OR 'methyl ionone':ti,ab,kw OR 'isobornyl acetate':ti,ab,kw OR 'hhcb':ti,ab,kw OR '1,3,4,6,7,8-hexahydro-4,6,6,7,8,8-hexamethylcyclopenta[g]-2-benzopyran':ti,ab,kw OR 'dpmi':ti,ab,kw OR 'diphenyl ether':ti,ab,kw OR 'pt-bucinal':ti,ab,kw OR 'ahtn':ti,ab,kw OR 'terpineol':ti,ab,kw OR 'pinene':ti,ab,kw OR 'methyl salicylate':ti,ab,kw OR 'methyl eugenol':ti,ab,kw OR 'linalool':ti,ab,kw OR 'limonene':ti,ab,kw OR 'hexyl cinnemal':ti,ab,kw OR 'eugenol':ti,ab,kw OR 'benzylacetate 5′:ti,ab,kw OR 'bbp':ti,ab,kw OR 'bp-3′:ti,ab,kw OR 'benzophenone-3′:ti,ab,kw OR 'd4′:ti,ab,kw OR 'octamethylcyclotetrasiloxane':ti,ab,kw OR 'd5′:ti,ab,kw OR 'decamethylcyclopentasiloxane':ti,ab,kw OR 'd6′:ti,ab,kw OR 'dodecamethylcyclohexylsiloxane':ti,ab,kw OR 'dehp':ti,ab,kw OR 'bis(2-ethylhexyl) phthalate':ti,ab,kw OR 'dpp':ti,ab,kw OR 'di-n-propyl phthalate':ti,ab,kw OR 'dichloromethane':ti,ab,kw OR 'formaldehyde':ti,ab,kw OR 'lye relaxer*':ti,ab,kw OR 'lye-relaxer*':ti,ab,kw OR 'sodium hydroxide':ti,ab,kw OR 'calcium hydroxide':ti,ab,kw OR 'guanidine carbonate':ti,ab,kw OR 'thio relaxer':ti,ab,kw OR 'thio relaxers':ti,ab,kw OR 'no lye relaxer*':ti,ab,kw OR 'thioglycolic acid salt*':ti,ab,kw OR 'diethylstilbestrol':ti,ab,kw OR 'polychlorinated biphenyls':ti,ab,kw OR 'dioxin':ti,ab,kw OR 'ultraviolet filter*':ti,ab,kw OR 'uv filter*':ti,ab,kw) AND ('hair'/exp OR 'hair':ti,ab,kw) AND ('endocrine disruptor'/exp OR 'gestagen'/exp OR 'estrogen'/exp OR 'gynecologic disease'/exp OR 'leiomyoma'/exp OR 'endocrine disrupt*':ti,ab,kw OR 'estrogen*':ti,ab,kw OR 'progest*':ti,ab,kw OR 'gestagen*':ti,ab,kw OR ((hippo NEAR/3 pathway):ti,ab,kw) OR 'hippo signaling pathway*':ti,ab,kw OR 'hormone pathway*':ti,ab,kw OR 'gynecologic condition*':ti,ab,kw OR 'gynecologic morbidit*':ti,ab,kw OR 'fibroid*':ti,ab,kw OR 'fibroma*':ti,ab,kw OR 'fibroid tumor*':ti,ab,kw OR 'fibromyoma*':ti,ab,kw OR 'myoma*':ti,ab,kw OR 'leiomyoma*':ti,ab,kw OR 'leiomyomata*':ti,ab,kw)
Scopus	Association of use of Hair Products and various benign and Malignant Gynecological conditions.	(TITLE-ABS-KEY("Progest*" OR "Estrogen*" OR "Leiomyoma" OR (hippo W/3 pathway) OR "hippo signaling pathway*" OR "hormone pathway*" OR "gynecologic condition*" OR "gynecologic morbidit*" OR "fibroid*" OR "fibroma*" OR "Fibroid Tumor*" OR "fibromyoma*" OR "myoma*" OR "leiomyoma*" OR "leiomyomata*")) AND ((TITLE-ABS-KEY(Preparations OR parabens OR phthalates OR "Phthalic Acids" OR lotion* OR relaxer* OR straightener* OR "octyl dimethyl" OR octinoxate OR "benzophenone-3″ OR "benzophenone-2″ OR "benzophenone-1″ OR benzophenone OR cyclosiloxanes OR dodecamethylcyclohexylsiloxane OR decamethylcyclopentasiloxane OR octamethylcyclotetrasiloxane OR "glycol ether*" OR "2,2-butoxyethoxyethanol" OR "2,2-ethoxyethoxyethanol" OR "2,2-methoxyethoxyethanol" OR "2-benzyloxyethanol" OR "2-phenoxyethanol" OR "2-butoxyethanol" OR "Alkylphenol" OR "nonylphenol diethoxylate" OR "nonylphenol monoethoxylate" OR "4-t-nonylphenol" OR "octylphenol diethoxylate" OR "octylphenol monoethoxylate" OR "4-t-octylphenol 6″ OR "Ethanolamines" OR "ethanolamine" OR "diethanolamine" OR "monoethanolamine" OR "triclosan" OR "o-phenylphenol" OR "bisphenol A" OR "BPA" OR "BPAs" OR "phthalates" OR "diethyl phthalate" OR "di-n-propyl phthalate" OR "S-7 di-n-octyl phthalate" OR "di-n-hexyl phthalate" OR "di-n-butylphthalate" OR "di-isononyl phthalate" OR "di-isobutyl phthalate" OR "di-cyclohexyl phthalate" OR "benzylbutyl phthalate" OR "bis(2-ethylhexyl) phthalate" OR "bis(2-ethylhexyl) adipate" OR "monobutyl phthalate" OR "mono(2-ethylhexyl) phthalate" OR "monoethylhexyl phthalate" OR "parabens" OR "butyl paraben" OR "ethyl paraben" OR "methyl paraben" OR "nonylphenols" OR "asthma associated chemical*" OR "fragrance*" OR "perfume*" OR "diethyl phthalate" OR "DEP" OR "phenethyl alcohol" OR "musk xylene" OR "musk ketone" OR "methyl ionone" OR "isobornyl acetate" OR "HHCB" OR "1,3,4,6,7,8-hexahydro-4,6,6,7,8,8-hexamethylcyclopenta[g]-2-benzopyran" OR "DPMI" OR "diphenyl ether" OR "pt-bucinal" OR "AHTN" OR "terpineol" OR "pinene" OR "methyl salicylate" OR "methyl eugenol" OR "linalool" OR "limonene" OR "hexyl cinnemal" OR "eugenol" OR "benzylacetate 5″ OR "BBP" OR "BP-3″ OR "benzophenone-3″ OR "D4″ OR "octamethylcyclotetrasiloxane" OR "D5″ OR "decamethylcyclopentasiloxane" OR "D6″ OR "dodecamethylcyclohexylsiloxane" OR "DEHP" OR "bis(2-ethylhexyl) phthalate" OR "DPP" OR "di-n-propyl phthalate" OR "Dichloromethane" OR "formaldehyde" OR "lye relaxer*" OR "lye-relaxer*" OR "sodium hydroxide" OR "calcium hydroxide" OR "guanidine carbonate" OR "thio relaxer" OR "thio relaxers" OR "no lye relaxer*" OR "thioglycolic acid salt*" OR "diethylstilbestrol" OR "polychlorinated biphenyls" OR "dioxin" OR "ultraviolet filter*" OR "UV filter*")) AND (TITLE-ABS-KEY ("hair")))
PubMed	Association of use of Hair Products and various benign and Malignant Gynecological conditions.	("Hair Preparations"[mh] OR (("Parabens"[mh] OR "Phthalic Acids"[mh] OR "lotion*"[tw] OR "relaxer*"[tw] OR" straightener*"[tw] OR "octyl dimethyl"[tw] OR "octinoxate"[tw] OR "benzophenone-3″[tw] OR "benzophenone-2″[tw] OR "benzophenone-1″[tw] OR "benzophenone"[tw] OR "cyclosiloxanes"[tw] OR "dodecamethylcyclohexylsiloxane"[tw] OR "decamethylcyclopentasiloxane"[tw] OR "octamethylcyclotetrasiloxane"[tw] OR "glycol ether*"[tw] OR "2,2-butoxyethoxyethanol"[tw] OR "2,2-ethoxyethoxyethanol"[tw] OR "2,2-methoxyethoxyethanol"[tw] OR "2-benzyloxyethanol"[tw] OR "2-phenoxyethanol"[tw] OR "2-butoxyethanol"[tw] OR "Alkylphenol"[tw] OR "alkylphenol"[tw] OR "nonylphenol diethoxylate"[tw] OR "nonylphenol monoethoxylate"[tw] OR "4-t-nonylphenol"[tw] OR "octylphenol diethoxylate"[tw] OR "octylphenol monoethoxylate"[tw] OR "4-t-octylphenol 6″[tw] OR "Ethanolamines"[tw] OR "ethanolamine"[tw] OR "diethanolamine"[tw] OR "monoethanolamine"[tw] OR "triclosan"[tw] OR "o-phenylphenol"[tw] OR "bisphenol A"[tw] OR "BPA"[tw] OR "BPAs" OR "phthalates"[tw] OR "diethyl phthalate"[tw] OR "di-n-propyl phthalate"[tw] OR "S-7 di-n-octyl phthalate"[tw] OR "di-n-hexyl phthalate"[tw] OR "di-n-butylphthalate"[tw] OR "di-isononyl phthalate"[tw] OR "di-isobutyl phthalate"[tw] OR "di-cyclohexyl phthalate"[tw] OR "benzylbutyl phthalate"[tw] OR "bis(2-ethylhexyl) phthalate"[tw] OR "bis(2-ethylhexyl) adipate"[tw] OR "monobutyl phthalate"[tw] OR "mono(2-ethylhexyl) phthalate"[tw] OR "monoethylhexyl phthalate"[tw] OR "parabens"[tw] OR "butyl paraben"[tw] OR "ethyl paraben"[tw] OR "methyl paraben"[tw] OR "nonylphenols"[tw] OR "asthma associated chemical*"[tw] OR "fragrance*"[tw] OR "perfume*"[tw] OR "diethyl phthalate"[tw] OR "DEP"[tw] OR "phenethyl alcohol"[tw] OR "musk xylene"[tw] OR "musk ketone"[tw] OR "methyl ionone"[tw] OR "isobornyl acetate"[tw] OR "HHCB"[tw] OR "1,3,4,6,7,8-hexahydro-4,6,6,7,8,8-hexamethylcyclopenta[g]-2-

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(*continued*)

Data Base	Concept	Search Statements
		benzopyran"[tw] OR "DPMI"[tw] OR "diphenyl ether"[tw] OR "pt-bucinal"[tw] OR "AHTN"[tw] OR "terpineol"[tw] OR "pinene"[tw] OR "methyl salicylate"[tw] OR "methyl eugenol"[tw] OR "linalool"[tw] OR "limonene"[tw] OR "hexyl cinnemal"[tw] OR "eugenol"[tw] OR "benzylacetate 5″[tw] OR "BBP"[tw] OR "BP-3″[tw] OR "benzophenone-3″[tw] OR "D4″[tw] OR "octamethylcyclotetrasiloxane"[tw] OR "D5″[tw] OR "decamethylcyclopentasiloxane"[tw] OR "D6″[tw] OR "dodecamethylcyclohexylsiloxane"[tw] OR "DEHP"[tw] OR "bis(2-ethylhexyl) phthalate"[tw] OR "DPP"[tw] OR "di-n-propyl phthalate"[tw] OR "Dichloromethane"[tw] OR "formaldehyde"[tw] OR "lye relaxer*"[tw] OR "lye-relaxer*"[tw] OR "sodium hydroxide"[tw] OR "calcium hydroxide"[tw] OR "guanidine carbonate"[tw] OR "thio relaxer"[tw] OR "thio relaxers"[tw] OR "no lye relaxer*"[tw] OR "thioglycolic acid salt*"[tw] OR "diethylstilbestrol"[tw] OR "polychlorinated biphenyls"[tw] OR "dioxin"[tw] OR "ultraviolet filter*"[tw] OR "UV filter*"[tw]) AND ("hair"[tw] OR "Hair"[mh])) AND ("Endocrine Disruptors"[mh] OR "Progestins"[mh] OR "Estrogens"[mh] OR "Genital Diseases, Female"[mh] OR "Leiomyoma"[mh] OR "endocrine disrupt*"[tw] OR "Estrogen*"[tw] OR "Progest*"[tw] OR "Gestagen*"[tw] OR "hippo pathway"[tiab:~3] OR "hippo signaling pathway*"[tw] OR "hormone pathway*"[tw] OR "gynecologic condition*"[tw] OR "gynecologic morbidit*"[tw] OR "fibroid*"[tw] OR "fibroma*"[tw] OR "Fibroid Tumor*"[tw] OR "fibromyoma*"[tw] OR "myoma*"[tw] OR "leiomyoma*"[tw] OR "leiomyomata*"[tw])

Appendix 2. . Criteria for inclusion and exclusion of studies

	Inclusion Criteria	Exclusion Criteria
Populations	Females diagnosed with gynecological condition	None
Symptom Specificity	Studies must be measuring at least one hair product associated with any gynecological condition risk	Studies lacked any measurement of quality of life as related to menstruation and the social determinants of health.
Results	Studies with quantitative measurement of desired symptoms.	Studies which lack measurement of the desired symptoms.
Study Design	Case-control studies, cohort studies, cross-sectional studies	Systematic reviews, case reports, non-scientific papers (political, activism, opinion)
Language	English-language publication	Non-English-Language Publication

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Glossary

Hair dye: Colorants, intended to color certain parts of the body by reflection or absorption of visible light [48]
Hair relaxer: Lotion or cream used to smooth out hair or straighten curls [49].
Hair oils: Gel-like or solid, petroleum-derived product with an oily consistency used as an emollient for the scalp or hair [35]
Deep conditioners: Water and oil-based moisturizer made for long-term application and used to restore moisture after shampooing [35].
Perms: Chemicals intended to change the straightness of the hair or natural curliness for a prolonged period of time [35].