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REVIEW ARTICLE

Association of hairdressing with cancer and reproductive diseases: A systematic review

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Abstract

Objectives: To review recent epidemiological studies investigating carcinogenic or reprotoxic effects among hairdressers who seem to be at greater risk for systemic adverse effects of chemicals released from hair care products than consumers.

Methods: A systematic review according to the PRISMA-P guidelines was performed and included studies published from 2000 to August 2021, in which cancer or adverse reproductive effects were diagnosed in 1995 and onward. Data were synthetized qualitatively due to the small number of studies, heterogeneity of study designs, outcomes, and methods.

Results: Four studies investigating cancer frequencies and six studies investigating effects on reproduction among hairdressers were identified. All were of good quality and with low risk of bias. Only one of the four studies found an increased risk of cancer reporting nine times higher odds for bladder cancer in hairdressers than the population-based controls. Three other studies investigating bladder and lung cancer, and non-Hodgins lymphoma did not find an increased risk in hairdressers. Regarding reprotoxic effects, numerous outcomes were investigated including menstrual disorders, congenital malformations, fetal loss, small-for-gestational age newborns, preterm delivery, and infertility. Increased risk was found for ventricular septal defect in newborns of fathers working as hairdressers.

Furthermore, several indices of poor neonatal or maternal health were significantly associated with mothers working as hairdresser.

Conclusions: Despite the scarce evidence that hairdressers are at increased risk of carcinogenic or reprotoxic effects related to their trade, such health risks cannot be ruled out. Therefore, preventive efforts to diminish occupational exposures to hairdressing chemicals should be targeted.

KEYWORDS

cancer, hairdressers, occupational, reproductive, review

1 | INTRODUCTION

Hairdressers are occupationally exposed to numerous chemicals in hairdressing products. Many of the chemicals are classified in regard to their toxicological properties and labeled according to the European Chemical Agency (ECHA) and the Regulation (EC) No 1272/2008 on classification, labeling, and packaging of substances and mixtures (CLP).[1,2] Typical hair cosmetic products and uses related to hairdressing are shown in Table 1.[2,3]

The risk for consumers using hairdressing products has been deemed acceptable by the Scientific Committee on Consumer Safety (SCCS), namely if pertinent restrictions according to Annex III of the Cosmetics Regulation EC 1223/2009 are applied.[4–6] The SCCS risk assessment however does not cover risk for professionals in daily contact with hairdressing products at work. A recent review comparing consumer and hairdressers' skin exposure levels concluded that the average frequency of use for consumers is severely underestimating exposure of hairdressers, with consequently higher risk of local and possibly systemic adverse effects.[7]

Hairdressing as occupation typically involves years of contact with numerous chemical mixtures, and according to the monograph published by the International Agency for Research on Cancer (IARC) in 2010, occupational exposure of hairdressers should be considered as probably carcinogenic (IARC group 2A).[8] In addition, three meta-analysis found significant 20%–30% higher risk for bladder cancer in hairdressers compared to the general population or non-exposed occupations.[9–11] Results of meta-analyses also indicate significantly increased frequency of other types of cancers in hairdressers, specifically laryngeal cancer[11,12] and multiple myeloma.[11] An association of the hairdressing occupation with lung cancer has not been consistent.[11,13] Carcinogenicity could be the result of a genotoxic mode of action. A meta-analysis showed increased micronucleus frequencies in buccal swabs from hairdressers compared to the non-exposed population.[14] Micronuclei may contain fragments produced from deoxyribonucleic acid (DNA) breakage or whole chromosomes produced by disruption of the mitotic apparatus, and therefore can be utilized as a surveying tool for genotoxic effects.[14] A recent study from Iran supports this finding.[15] In addition, a study from Brazil,[16] a country where hair straightening is popular,[17] found around 30% higher DNA damage among hairdressers compared to controls based on comet assay performed on blood samples.

TABLE 1 Main groups of hairdressing products and their properties

Hair product	Typical ingredients	Routes of exposure for hairdressers	Health hazards[a]
Oxidative hair dyes/colorants	Dye precursors *p*-phenylene diamine (PPD) or toluene-2,5-diamine (PTD)	Dermal and inhalation	Acutely toxic by ingestion, inhalation and skin contact, local irritation in contact with skin and eyes, sensitization after dermal contact
Perms and relaxing substances	Thioglycolic acid, its salts and esters	Dermal	
Hair bleaches	Persulfate salts	Dermal and inhalation	Acutely toxic by ingestion, inhalation, and in contact with skin, local irritation in contact with skin and eyes, sensitization after dermal contact, respiratory irritation and sensitization

[a]Source: Annex VI to Regulation (EC) No 1272/2008 of the European Parliament and of the Council of 16 December 2008 on classification, labeling, and packaging of substances and mixtures.

Interestingly, one study investigated associations of filaggrin gene variations with cancer-related DNA changes among hairdressers involved in frequent oxidative hair dying and bleaching (more than seven times per week).[19] With adjustment for glove use, these heavily exposed hairdressers who were also carriers of intragenic copy number variation resulting in reduced filaggrin levels in the skin had an increased risk for having methylation at one cancer-related genetic site (CDKN2A), indicating a possible increased risk for cancers.[19] Regarding reprotoxic effects, meta-analyses and a systematic review found an increased risk of infertility, time to pregnancy, embryotic, and fetal losses among hairdressers and cosmetologists when compared to the non-exposed population, and increased risk of preterm delivery and low-birth weight of their newborns.[19–21] On the other hand, one systematic review noted inconsistent results across the included studies regarding outcomes such as small for gestation age, low birth weight, and spontaneous abortions, but concluded nevertheless that pregnancy complications in hairdressers cannot be ruled out.[22]

The limitation of the above-mentioned reviews is that the included epidemiological studies spanned several decades, from 1950s until early 2000s. During this period ingredients in hair products changed significantly. In the 1980s, mutagenic or carcinogenic aromatic amines were banned for use in hair dyes.[8,9] There is also a problem of long latency time for the development of cancer, which can complicate an interpretation of a review covering broad time period. For example, the reported average latency periods for bladder cancer development after the start of occupational exposure to a carcinogenic substance were between 14 and 27 years, and mostly close to 20 years.[23–25] In addition, examining a recent time period would also more clearly point out the associations of currently relevant occupational exposure with adverse effects on reproduction. Therefore, we conducted a systematic review of epidemiological studies published in the last two decades, investigating carcinogenic and reprotoxic effects among hairdressers to provide an updated review.

2 | METHODS

2.1 | Search strategy

This study is part of a project reviewing the toxicity of important hair and nail cosmetic ingredients in hairdressers. In this review, the focus was on carcinogenic and reprotoxic effects. A detailed protocol for systematic reviews performed within this project has previously been published[26] and registered under the PROSPERO registration number CRD42021238118.[27] It is based on the Preferred Reporting Items for Systematic Reviews and Meta-Analysis Protocols (PRISMA-P).[28] We systematically searched the electronic databases MEDLINE, Web of Science - core collection, and Cochrane Library, in addition to Scientific Committee on Consumer Safety (SCCS) opinions, and toxicological dossiers of the German Committee for the determination of occupational exposure limits ('MAK-Commission'). We searched for publications in English, published in 2000 or later, reporting results of any type of epidemiological observational studies investigating systemic effects of oxidative hair dyes or their components, persulfate salts, thioglycolic acid salts, and hairdressing exposure in general, including case–control studies, prospective and retrospective cohort studies. References of publications were checked for possible additional literature. Searches were performed from April to August 2021. As this work was a systematic review of published primary studies, no approval from an ethical review board was required.

The full search string used is presented in Appendix 1. Substances included in the systematic review were the most indicative ingredients in the most relevant groups of hairdressing products:

- Oxidative hair dyes/colorants: p-Phenylenediamine (PPD; CAS no. 106-50-3) and its salts (CAS no. 624-18-0, 16245-77-5), toluene-2,5-diamine (PTD; CAS no. 9570-5) and its sulfate (CAS no. 615-50-9), and 2-methoxymethyl-PPD (mePPD; CAS no. 33790636-2);
- Bleaches: Persulfate salts: ammonium, APS, CAS no. 7727-54-0; potassium, PPS, CAS no. 7727-21-1; sodium, SPS, CAS no. 7775-27-1;
- Perms and relaxing substances: Salts and esters of thioglycolic acid: glyceryl thioglycolate (GMTG; CAS no. 30618-84-9), ammonium thioglycolate (ATG; CAS no. 5421-46-5).

The keywords for systemic effects covered cancerogenic and genotoxic properties, reproductive health indicators, and various adverse pregnancy outcomes (Appendix 1).

2.2 | Publication selection

The process of publication selection was performed in accordance with the PRISMA-P guidelines (Figure 1).[28] Two researchers (Ž.B. and J.M.) independently screened publications (2000–2021) listed in the search results by title and abstract for any relevant product identifiers and toxicological endpoints. Because of numerous epidemiological studies investigating carcinogenic or reprotoxic effects among hairdressers over several decades, for this study we selected only those in which cancer or adverse

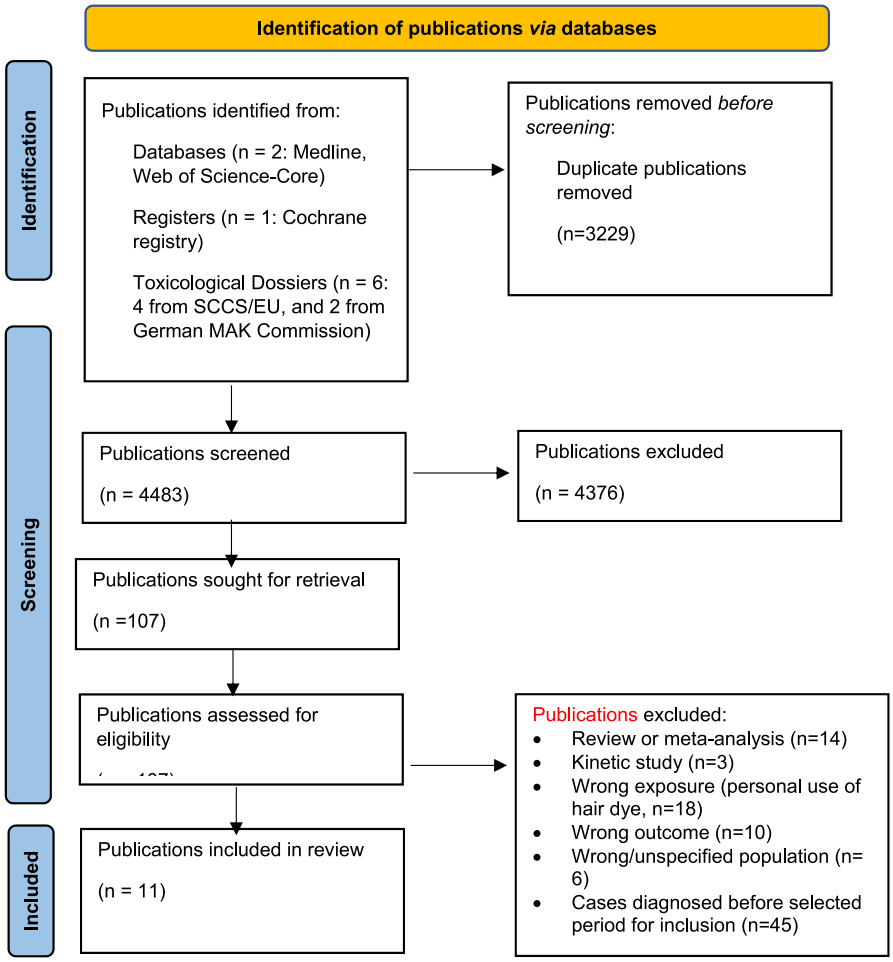

FIGURE 1 PRISMA flow-chart (Page 2021).
FROM: PAGE MJ, MCKENZIE JE, BOSSUYT PM, BOUTRON I, HOFFMANN TC, MULROW CD, ET AL. THE PRISMA 2020 STATEMENT: AN UPDATED GUIDELINE FOR REPORTING SYSTEMATIC REVIEWS. BMJ 2021;372:N71. DOI: HTTPS://DOI.ORG/10.1136/BMJ.N71

reproductive effect were diagnosed in a period starting from 1995 onwards, so that the more current exposure conditions were better reflected. One additional study was included although the data collection was done by questionnaire on fertility outcomes in any pregnancy, which was sent out in 2003 to hairdressers born in 1960 or later.[29] The reason was that this was the only identified study published within the selected period which investigated associations of adverse outcomes with frequency of various hair treatments involving chemicals at work (working with oxidative and non-oxidative hair coloring formulations permanent waving solutions and their setting solutions, and hair bleaches). All other studies explored adverse outcomes with hairdressing exposure in general.

2.3 | Data extraction

Two reviewers (Ž.B., J.M.) independently extracted the data from studies meeting the inclusion criteria using publication record forms. Data extracted were publication ID, country, and year of study execution, study design, population involved, number of participants, method of recruitment, methods, and main results. Any type of adverse outcome related to carcinogenicity or reproductive toxicity was considered important and provided data were extracted, which commonly included frequencies of specific types of cancers, frequencies of congenital malformations, fetal loss, preterm births, low birth weight, other poor neonatal health indicators such as low Apgar (Appearance, Pulse, Grimace, Activity, and Respiration) score, maternal perinatal adverse events such as preeclampsia, any menstrual disorder, and infertility.

2.4 | Quality assessment

Criteria for the evaluation of quality and risk of bias for this systematic review were made by authors using three sources: (i) mixed methods research appraisal[30]; (ii) Cochrane collaboration[31]; (iii) working group of the US EPA.[32] Criteria consisted of three parts regarding appropriate design, sampling, and sample, justification of methodology (validity and standards), and justification/presentation of results. A maximal score of 15 was possible for clinical observational studies. Criteria are described in detail in Appendix 2. A score yielding a proportion ≥70% (i.e. ≥10.5 points) was considered good quality and a

score <70% to be of lower quality. Two reviewers who independently extracted the data from included studies also assessed the quality of studies, including the risk of bias.

2.5 | Data synthesis

Characteristics and main findings of included studies were summarized in tables following IARC method of reporting the study location and period, characteristics of cases/controls, or cohort description, exposure assessment, exposure/outcome categories, exposed cases, metrics of relative risk such as odds ratio (OR) or risk ratio (RR) with 95% confidence intervals (CI), and adjustment factors.[8] Because of the diversity of relevant outcomes and the limitation to include only recent studies, it was not feasible to pool results quantitatively. Instead, results, including quantifications from single studies considered sufficiently valid, were synthetized by textual explanation, addressing the sources of heterogeneity and providing an overall conclusion.

3 | RESULTS

3.1 | Carcinogenic effects

To check if hairdressing occupation is still significantly associated with cancer morbidity, primary studies which included cancer patients diagnosed from 1995 onward were analyzed (Table 2, $N = 4$).[33–37] In summary, three case–control studies from the EU[33,36,37] found no significant association between lung cancer and bladder cancer. In a case–control study from New Zealand, hairdressers had nine times higher odds for bladder cancer than population-based controls, with adjustment for sex, age, smoking, occupational status, and ethnicity.[34] In the same study an employment in hairdressing industry was associated with five times higher odds than controls.[34] However, these results are based on the comparison of only six cancer cases among hairdressers with three cases among controls (OR 9.15, 95% CI 1.60–52.22), and seven cancer cases among those employed in the hairdressing industry and five among controls (OR 5.35, 95% CI 1.37–20.9). Authors suggested that the observed increased risk for bladder cancer in hairdressers is causally related to the exposure to aromatic amines, which are common ingredients of permanent hair dyes. In the same New Zealand study, the risk of non-Hodgkin's lymphoma was not significantly elevated among hairdressers, beauty therapists, and related workers.[35] All of the studies were of good quality, with sufficiently detailed description of cases/controls, data collection, statistical analysis, and completely documented results. Low risk of bias was detected; two of the four studies were register-based[34–36] and the two hospital-based studies[33,37] describing pre-defined criteria for selection of cases and provided response rates concerning participation.

There were no epidemiological studies identified which investigated association of cancer incidence and specific hairdressing tasks such as hair dyes, bleaching, or waving.

3.2 | Reprotoxic effects

To determine if hairdressing occupation is still significantly associated with adverse effects on reproduction, studies which included effects diagnosed from 1995 onward were analyzed (Table 3, $N = 6$).[38–43] In summary, none of six studies with various designs (case–control, retrospective cohort, prospective cohort, and cross-sectional) investigating outcomes including menstrual disorders, congenital malformations, fetal loss, small-for-gestational age children, and preterm delivery showed a significantly increased risk in hairdressers. However, in one case–control study from the United States of America (USA) a borderline significance was found for congenital malformations (ventricular septal defect in newborns),[38] based on 2 cases of ventricular septal defect (VSD) in newborns of 26 fathers employed in hairdressing (OR 2.7, 95% CI 1.0–7.5). Similarly, some indices of poor neonatal or maternal health were found to be associated with maternal occupation as a hairdresser in one cohort study from the USA.[39] Specifically, newborns of mothers employed as hairdressers had significantly higher odds in comparison with control group of mothers employed as real-estate agents for low 1-min Apgar score (Appearance, Pulse, Grimace, Activity, and Respiration score; OR 1.33, 95% CI 1.09–1.63), low 5-min Apgar score (OR 2.02, 95% CI 1.04–3.94), pregnancy-induced hypertension (OR 1.34, 95% CI 1.01–1.76), slowed labor with delayed delivery (OR 1.31, 95% CI 1.12–1.54), precipitous labor (OR 1.52, 95% CI 1.07–2.15), and postpartum hemorrhage (OR 2.12, 95% CI 1.26–3.58). However, these differences were not significant when a population-based control group was employed in that same study. Regarding infertility, in the Danish study, none of the investigated types of female infertility (associated with anovulation of tubal, uterine, cervical, or other origin, or unspecified) was significantly associated with hairdressing occupation.[40] The overall RR (95%CI) for infertility due to any reason was 0.93 (0.72–1.18) when hairdressers were compared to a reference population of all economically active women in Denmark aged 20–44 years, and 1.01 (0.77–1.29) in comparison to women employed as shop

TABLE 2 Studies investigating associations of hairdressing occupation with various types of cancers diagnosed 1995 onward ($N = 4$ studies, $N = 5$ publications)

Reference: study location, period	Study design	Characteristics of cases	Characteristics of controls	Exposure assessment
Consonni et al. (2010)[33]: Italy, 2002–2005	Case control	Incident lung cancer cases (1015 men and 379 women; any stage of primary cancer of the trachea, bronchus, and lung) admitted to 13 hospitals in Northern Italy; aged 35–79 years	Randomly sampled control individuals (1171 men and 471 women) from population databases, frequency matched to cases by residence, sex, and age	Computer-assisted interview
Dryson et al. (2008),[34] Mannetje et al. (2008)[35]: New Zealand, 2003–2004	Case–control	213 **bladder cancer** cases were reported to the New Zealand Cancer Registry; aged 25–70 years, 54% men 291 incident cases of non-Hodgkin's lymphoma (NHL) reported to the same Register; aged 25–70 years, 54% men	471 controls randomly selected from a national electoral roll, frequency matched to cases by age	Face-to-face interview by a trained interviewer
Guida et al. (2011)[36]: France, 2001–2007	Case–control	648 incident primary lung cancers, regardless of histological type, diagnosed in 10 of 11 French administrative departments with a general cancer registry; women aged 18 to 75 years	775 population controls with no history of previous respiratory cancer, randomly selected in the same departments as cases through incidence density sampling, frequency matched to cases by age, sex, department, socioeconomic status	Face to-face interviews using standardized questionnaire
Samanic et al. (2008)[37]: Spain, 1998–2000	Case–control	1219 cases of urothelial cell carcinoma of the bladder or carcinoma in situ of the bladder, including ureteric orifice and urachus, diagnosed in 18 participating hospitals in Spain; aged 21–80 years, 88% men	1271 control individuals selected from patients admitted to the same hospital for diseases/conditions unrelated to the studied exposures, matched to cases by age, sex, race/ethnicity, and hospital	Computer-assisted personal interview

[a]Maximum score = 15; scores ≥70% of maximum score are in bold; OR = odds ratio; 95% CI = 95% confidence interval.

assistants with the same age range.[40] All of these studies were of good quality, with sufficiently detailed description of cases/controls or a cohort, and data collection. The risk of bias was not detected. Specifically, four of the six studies were register-based,[38–40,43] and the other two, one hospital-based[41] and one performed in hairdressing salons,[42] described the process of recruitment in detail, including inclusion criteria and response rates.

Exposure categories	Exposed cases	OR (95% CI)	Adjustment factors	Comments	Quality assessment Total score[a]
Employed as a hairdresser, barber, beautician, or related worker	12 men, 13 women	Men: 1.63 (0.52–5.14) Women: 2.00 (0.57–7.04)	Area, age, smoking, number of jobs, and education		**12**
• **Hairdressers** • **Industrial classification of "hairdressing and beauty salons"** Hairdressers, beauty therapists, and related workers	6 7 4	**9.15 (1.60–52.22)** **5.35 (1.37–20.9)** 1.09 (0.27 to 4.35)	Sex, age group, smoking status, Maori ethnicity, and occupational status	These were linked case–controls studies which have used the same group of population controls. There were no consistent patterns by the duration of employment (1–2 years, 2–10 years, more than 10 years) for both type of cancer.	**14**
Employed as a hairdresser	16	2.0 (0.7–5.7)	Age at interview, department, lifelong cigarette smoking, and number of jobs held	Regarding hairdressers, OR and 95% shown only for women, among men presumably also non-significant association of smaller magnitude	**14**
Employed as a barber/hairdresser	12	1.24 (0.51 to 3.01)	Age, hospital region, smoking duration, and ever being employed in a high-risk occupation for bladder cancer which included a priori high-risk jobs authors identified in the literature, and jobs within that study which were either statistically significantly associated with bladder cancer or had an OR of 1.5 or higher	Three hairdressers/barbers worked for <10 years and 9 for 10 and more years. Duration of employment had no significant influence on the association: 0.93 (0.19–4.52) for <10 years and 1.42 (0.48–4.18) for 10 or more years	**12.5**

In the selected period of publication (2000–2021), there were no epidemiological studies investigating the association of specific hairdressing tasks exposure with any adverse effects on reproduction such as congenital malformations, maternal and neonatal health, and fertility, which were diagnosed from 1995 onwards, in contrast to above-mentioned publications addressing hairdresser exposure as a whole. There was one study of good quality without noted risk of bias investigating fecundability among Swedish hairdressers in regard to the reported number of

TABLE 3 Studies investigating associations of hairdressing occupation with reproductive effects ($N = 6$ studies, $N = 6$ publications)

First author, year of publication	Study design	Characteristics of cases	Characteristics of controls	Exposure assessment	Exposure categories
Congenital malformations					
Desrosiers et al. (2012)[38]: USA, 1997–2004	Case–control study	9998 cases with one or more major birth defect identified by 10 participating USA state birth defect surveillance systems	4066 newborns randomly selected in each state among live births without major defects from either hospital records or birth certificates	Telephone interview with mothers	Hairdressing or cosmetologist occupation of father ($N = 26$; 0.3%)
Herdt-Losavio et al. (2009)[39]: USA, 1997–2003	Retrospective cohort study	Cohort description: 15 003 newborns of mothers who worked as cosmetologists (defined as having a cosmetologist license in 2003) born in New York from 1997–2003		New York City Congenital Malformation registry, and state birth records which include data on neonatal health indicators and maternal pregnancy risk factors	Congenital malformation of: male reproductive tract Genitourinary Hearts Eye/ear Respiratory Digestive tract Neural tubes Clefts Musculoskeletal
Nguyen et al. (2007)[41]: Norway, 1996–2001	–control study	432 infants born with an isolated orofacial cleft during the period 1996 to 2001 and referred for surgery in two specialized centers covering all Norway; among them 314 were with cleft lip with or without palate (CLP) and 118 with cleft palate only (CPO)	763 control infants randomly chosen from all Norwegian live births, using Medical Birth Registry of Norway	Mailed questionnaire	Hairdressing occupation of mother
Zhu et al. (2006)[43]: Denmark, 1997–2003	Prospective cohort study	Among the 88 915 pregnancies included in Danish National Birth Cohort study 1997–2003, for this study authors identified 571 pregnancies of hairdressers ($N = 550$, 70% <30 years, 30% ≥30 years) and 3317 pregnancies of shop assistants or sales assistants (unexposed group, $N = 3216$, 73% <30 years, 27% ≥30 years)		Data from Danish National Birth Cohort study, collected 1997–2003 using computer-assisted telephone interviews	All malformations "Major" malformations

N of cases among exposed	OR or RR (95% CI)	Adjustment factors	Comments	Quality assessment Total score[†]
Choanal atresia 1	ORs: 2.0 (0.7–5.2)	Maternal age at delivery, maternal race/ethnicity, maternal education, maternal smoking, maternal alcohol use, maternal vitamin/folic acid use, and maternal residence at delivery		**12**
Limb deficiency, longitudinal preaxial 2	2.0 (0.9–4.8)			
Gastroschisis 3	2.0 (0.9–4.3)			
Ventricular septal defect, conoventricular 2	**2.7 (1.0–7.5)**			
Atrioventricular septal defect 2	2.2 (0.9, 5.4)			
92	ORs: vs. realtors and vs. general population, respectively: 0.80 (0.53–1.20) 1.19 (0.88–1.61)	Race, ethnicity, body mass index, age, smoking, participation in any aid program, education, alcohol use, prenatal care, maternal diabetes, residential county with high number of hazardous waste sites, and parity	In paper Herdt-Losavio et al. (2011),[50] it was described that cosmetologists, selected for that nested case–control study from this study, also performed the hairdressing tasks: 64% reported that they daily bleach, dye, tint, or highlight hair. Realtors (control group): licensed real-estate agents and real-estate brokers. The authors stated that realtors have similar education requirements and large proportion of females.	**13.5**
174	0.71 (0.51–1.01) 1.09 (0.84–1.41)			
147	0.82 (0.55–1.21) 1.05 (0.79–1.40)			
6	1.12 (0.13–9.81) 0.71 (0.21–2.33)			
22	1.35 (0.39–4.68) 1.24 (0.59–2.59)			
58	1.10 (0.53–2.28) 1.17 (0.73–1.88)			
24	1.38 (0.40–4.72) 0.70 (0.38–1.32)			
18	3.62 (0.48–27.58) 1.16 (0.54–2.52)			
92	0.86 (0.52–1.43) 0.83 (0.59–1.17)			
Isolated CLP: 4 Isolated CPO: 1	ORs: Isolated CLP: 4.80 (0.99–23) Isolated CPO: 2.30 (0.21–25)	Women's smoking, drinking, education, parity, age, folic acid intake (dietary and supplement), father's age, calendar year of child's birth and whether the parents were married/living together		**14**
29	ORs: 0.8 (0.6–1.2)	Maternal age, gravidity, history of spontaneous abortion, prepregnancy body mass index, smoking, and alcohol consumption	Major malformations were considered according to International Classification of Diseases, version 10, excluding accessory auricle, undescended testes, hip dislocation, and pigmented nevus. One hundred forty hairdressers worked for <35 h per week, and 410 for 35 h or more. No differences were found among the hairdressers with different weekly work hours.	**14**
24	0.9 (0.6–1.4)			

(Continues)

TABLE 3 (Continued)

First author, year of publication	Study design	Characteristics of cases	Characteristics of controls	Exposure assessment	Exposure categories
Poor neonatal health indicators and maternal perinatal adverse effects					
Herdt-Losavio et al. (2009)[39]: USA, 1997–2003	Retrospective cohort study	Cohort description: 15 003 newborns of mothers who worked as cosmetologists (defined as having a cosmetologist license in 2003) born in New York from 1997–2003		New York City Congenital Malformation registry, and state birth records which include data on neonatal health indicators and maternal pregnancy risk factors	**Other poor neonatal health indicators: Low 1-min Apgar score (<7)** **Low 5-min Apgar score (<7)** **Respiratory distress syndrome** **Intubation** **Maternal perinatal adverse events: Preeclampsia** **Pregnancy-induced hypertension** Placenta previa Abrubtio placenta Premature rupture of membranes **Prolonged rupture of membranes** **Failure to progress** Prolonged labor **Precipitous labor** **Postpartum hemorrhage**
Zhu et al. (2006)[43]: Denmark, 1997–2003	Prospective cohort study	Among the 88 915 pregnancies included in Danish National Birth Cohort study 1997–2003, for this study authors identified 571 pregnancies of hairdressers ($N = 550$, 70% <30 years, 30% ≥30 years) and 3317 pregnancies of shop assistants or sales assistants (unexposed group, $N = 3216$, 73% <30 years, 27% ≥30 years)		Data from Danish National Birth Cohort study, collected 1997–2003 using computer-assisted telephone interviews	Fetal loss Preterm infant Very preterm infant Small-for-gestational age
Infertility and menstrual disorders					
Hougaard et al. (2006)[40]: Denmark, 1998–2002	Prospective cohort study	4113 women aged 20–44 years at the baseline (1998), registered as economically active, with "bath assistant, hairdresser, barber, beautician and masseur" and "hairdressing saloons "as their main occupation and industry, and referent population of all economically active women in Denmark aged 20–44 years at baseline (number unreported, calculated based on reported number of events and group frequencies: 710.442)		Danish Occupational Hospitalization Register (OHR; record linkage between three national registers—the Central Person Register, the Hospital Register and the Employment Classification Module)	Female infertility, overall Specific types: Associated with anovulation Of tubal origin Uterine origin Cervical origin of other origin Unspecified type of infertility

N of cases among exposed	OR or RR (95% CI)	Adjustment factors	Comments	Quality assessment Total score[†]
863	ORs: vs. realtors and vs. general population, respectively: **1.33 (1.09–1.63)** 0.92 (0.82–1.03)	Race, ethnicity, body mass index, age, smoking, participation in any aid program, education, alcohol use, prenatal care, maternal diabetes, residential county with high number of hazardous waste sites, and parity	In paper Herdt-Losavio et al. (2011),[50] it was described that cosmetologists, selected for that nested case–control study from this study, also performed the hairdressing tasks: 64% reported that they daily bleach, dye, tint, or highlight hair. Realtors (control group): licensed real-estate agents and real-estate brokers. The authors stated that realtors have similar education requirements and large proportion of females.	**13.5**
116	**2.02 (1.04–3.94)** 0.82 (0.60–1.12)			
137	1.53 (0.86–2.71) **0.60 (0.45–0.80)**			
146	**2.34 (1.21–4.51)** **0.76 (0.57–1.00)**			
233	1.06 (0.74–1.53) **0.76 (0.62–0.95)**			
464	**1.34 (1.01–1.76)** 0.94 (0.80–1.10)			
77	0.78 (0.46–1.31) 0.93 (0.63–1.37)			
109	0.98 (0.59–1.63) 0.83 (0.59–1.16)			
497	1.22 (0.95–1.57) 1.10 (0.94–1.29)			
363	**1.52 (1.11–2.09)** 1.10 (0.93–1.32)			
1423	**1.31 (1.12–1.54)** 1.00 (0.90–1.10)			
177	1.48 (0.96–2.30) 1.13 (0.88–1.45)			
297	**1.52 (1.07–2.15)** 0.96 (0.80–1.16)			
170	**2.12 (1.26–3.58)** 0.93 (0.73–1.18)			
5	ORs: 0.7 (0.3–1.8)	Maternal age, gravidity, history of spontaneous abortion, prepregnancy body mass index, smoking, and alcohol consumption	Preterm was considered <37 weeks, and very preterm birth <34 weeks of gestation. One hundred forty hairdressers worked for <35 h per week, and 410 for 35 h or more. No differences were found among the hairdressers with different weekly work hours.	**14**
29	1.0 (0.7–1.6)			
8	0.9 (0.4–2.1)			
57	1.0 (0.7–1.3)			
68	RR: 0.93 (0.72–1.18)	–	RRs with 95% were not presented in the paper, but we calculated them based on the reported frequencies of events and group sizes. Additionally, the authors reported adjusted RR for overall infertility only: 0.911 (95%CI 0.71–1.16) with adjustment for county, and 0.901 (0.70–1.14) for socioeconomic group. Comparison with additional control group was reported only for overall infertility: 1.01 (0.77–1.29) in comparison to 33 775 women employed as shop assistants with same age range	**12.5**
3	1.03 (0.33–3.22)			
8	1.08 (0.54–2.17)			
0	1.48 (0.09–23.87)			
0	9.09 (0.53–156.14)			
19	0.94 (0.60–1.47)			
38	0.90 (0.65–1.23)			

TABLE 3 (Continued)

First author, year of publication	Study design	Characteristics of cases	Characteristics of controls	Exposure assessment	Exposure categories
Ronda et al. (2009)[42]: 2006, Spain	Cross-sectional study	310 hairdressers recruited in hairdressing salons in Spain (age 30.3 ± 8.8 years) and 310 control office workers from a telecommunications company and the university from the same region (34.1 ± 8.3 years)		Questionnaire	Any menstrual disorder for which a participant received specialist treatment within last 12 month

treatments with hairdressing formulations performed per week.[29] The study included a cohort of women who had graduated from any of the 29 Swedish vocational schools for hairdressers between 1970 and 1995 and who were born in 1960 or later, with a subgroup of women working as hairdresser during the time when they were trying to conceive. The reference cohort consisted of women from the Swedish general population. Data on exposure and pregnancies were collected by mailed questionnaires. Comparing women working as hairdressers with participants from the general population, there was no significant difference in fecundability, with adjustment for birth control use, or frequency of miscarriages during the first planned pregnancy. The authors further sub-categorized the hairdressers according to specific work tasks (working with oxidative and non-oxidative hair coloring formulation, setting permanent waves, and hair bleaching). Compared to the general population, hairdressers setting permanent waves for more than four times per week had a significantly prolonged time to pregnancy (fecundability ratio 0.86 with 95% CI 0.76–0.97), similar to those bleaching hair for up to four times per week (0.88, 95% CI 0.78–0.99), dyeing with oxidative formulations for more than two times per week (0.83, 95% CI 0.73–0.94), and those dying with direct-acting dyes (0.86, 95% CI 0.76–0.96). On the other hand, a number of miscarriages in first planned pregnancy were not significantly different in regard to any task, with adjustment for year of birth, age at conception, performance of heavy lifts, use of oral contraceptives prior to pregnancy, menstrual cycle length prior to pregnancy, partner's smoking habits, and workplace smoking.

4 | DISCUSSION

The results of this systematic review, including studies from the last 25 years, do not clearly indicate that hairdressers are at risk of cancer and reproductive effects related to their trade, in contrast to conclusions of previous systematic reviews and meta-analyses which included studies spanning several earlier decades.

4.1 | Carcinogenic effects

Only one of the four included studies on cancers diagnosed in period 1995 onward found a significantly increased risk reporting nine-fold higher odds for bladder cancer in hairdressers from New Zealand.[34] However, absolute numbers of cases identified through the cancer registry were very low (six among hairdressers), with consequently very broad confidence intervals of the associations. The other identified study on bladder cancer,[37] which was conducted in Spain and hospital-based, did not find a significant association with the hairdressing profession. The New Zealand study on non-Hodgins lymphoma[35] and the two EU studies on lung cancer[33,36] also did not find increased odds among hairdressers when adjusting for smoking. In our review we, deliberately selected a rather short time span as in the last decades the composition of hair care products changed over time due to changes in regulatory policy, technical and product requirements, and availability and introduction of new ingredients.[44] The most prominent and relevant example was the discovery of in vitro mutagenic activity and in vivo carcinogenic activity of aromatic amines used in hair dye formulation in the mid-1970s which led to regulatory restrictions and prompted manufacturers to reformulate oxidative dye products during the late 1970s and early 1980s.[8,45] Previous meta-analyses and systematic reviews included studies on patients diagnosed with cancer from the 1950s until early 2000s. Bladder cancer was reported to be significantly associated with the hairdressing occupation in three meta-analyses, with a similar calculated summary (pooled) risk ratio for hairdressers: 1.23 (95% CI 1.11–1.37) in Reulen et al. (2008), 1.30 (95% CI 1.15–1.48) in Harling et al. (2010), and 1.30 (95% CI 1.20–1.42) in Takkouche et al. (2009).[9–11] Harling et al. (2010) found that working as a hairdresser for more than 10 years was associated with a summary risk ratio of 1.70 (95% CI 1.01–2.88).[9] The excess risk for hairdressers found in these analyses is lower than in the mentioned study we identified in the recent time period, which reported nine-fold higher odds for bladder cancer

N of cases among exposed	OR or RR (95% CI)	Adjustment factors	Comments	Quality assessment Total score[†]
17	OR: 2.17 (0.91–5.17)	Age and smoking	Hairdressers working in this profession for 10 or more years had significantly higher risk than controls for menstrual disorders and subfertility: 3.31 (1.34–8.17) and 3.27 (1.28–8.29), respectively. No significant associations with hours of work per week was found (≤40 or >40), overall mean (SD) was 43.5 (7.6) hours.	**14**

in hairdressers,[34] but for a rather small number of participants. Summary risk of bladder cancer was significantly higher for hairdressers in every stratified period of case ascertainment (<1980, 1980s, and >1990s) in the meta-analyses and similar in magnitude to overall risk ratio.[9–11] The highest risk was noted from the 1990s onwards.[9,10] Smoking was recognized as important confounder, but association with the hairdressing occupation remained significant even when including only smoking-adjusted data.[9,10] Even if the cancer incidence was not found to be high in our review, there are recent studies showing increased micronucleus frequencies, higher DNA damage, and cancer–related DNA changes in hairdressers compared to non-exposed population.[15,16,18] Previous studies identified also increased risk for skin cancer among hairdressers, specifically affecting the scalp and neck, but not clearly work-related.[46,47] We did not find more recent studies in this regard.

4.2 | Effects on reproduction

Similar to studies on carcinogenicity, only few of the reproductive studies noted significant associations between reprotoxic effects and the hairdressing trade. Among five types of congenital defects that were investigated, Desrosiers et al. (2012) found increased odds for the conoventricular septal defect if a father worked as a hairdresser, with adjustment for factors associated with the mother's health and residency, but not mother's occupation, which would have added more reliability to the finding.[38] In addition, the association was of borderline statistical significance, most probably due to the low number of cases which were identified through a state birth defect surveillance system. In other identified studies conducted in EU countries and the USA, birth defects were not significantly associated with the hairdressing trade,[39,41,43] as well as adverse fetal and neonatal outcomes such as fetal loss, preterm-infant and small-for gestational age,[43] female infertility[40] or menstrual disorders.[42] However, Herdt-Losavio et al. (2009) found significant associations of several poor neonatal health indicators and maternal perinatal adverse events with the hairdressing occupation of mothers in comparison to real-estate agents and brokers, with adjustment for factors associated with the mother's health,[39] but unfortunately not with occupational conditions such as prolonged standing, physical work, and heat exposure, which are known risk factors for reproductive outcomes.[48] Furthermore, the associations in that study were sensitive to the choice of the control group, and many lost significance or reversed direction in comparison to the other control group, which was the general population. Taken together, there is no clear indication that the hairdressing trade is still associated with adverse effects on reproduction, which is in contrast with previous studies. Most prominently, in two meta-analyses, one[19] which included studies conducted from the 1980s until 2000s, and the other,[20] which included studies conducted from the 1960s until 2000s, slightly increased overall risks (up to 20%) of several adverse reproductive outcomes among hairdressers were noted. The most consistent results were found for premature birth and low birth-weight, for which no significant associations were noted in the recent studies identified in our review.

None of the mentioned studies included in this review regarding carcinogenicity investigated associations with specific hairdressing tasks, while for reproductive outcomes one such study was found. In the Swedish study of Axmon et al. (2006), fecundability of hairdressers was significantly lower, meaning lower probability of achieving pregnancy within one menstrual cycle, in hairdressers in comparison to the general population.[29] This difference was associated with weekly frequency of hair-coloring with oxidative or non-oxidative acting dyes, hair bleaching, and hair waving. There was no significant difference in frequencies of miscarriages in that study with regard to specific hairdressing tasks. It is difficult to relate specific hairdressing tasks to risk levels because a hairdresser usually performs all tasks, including hair dyeing with oxidative or non-oxidative dyes, bleaching with persulfates and waving with thioglycolates, with more or less constant frequency.

The EU cosmetics regulation contains provisions on the use of substances with carcinogenic, mutagenic, or toxic for reproduction properties (CMR substances) in cosmetic products. As a general principle, substances classified as CMR Category 1A, 1B, or 2 are banned for use in cosmetic products under Part 3 of Annex VI to CLP Regulation EU 1272/2008. There are, however, some exceptions. For example, a substance classified in category 2 may be used in cosmetic products where the substance has been evaluated by the SCCS and found safe for consumers for use in cosmetic products, mostly below a given maximum use concentration (see Annex III to EC 1223/2009). This becomes even more important as an agreement to include reprotoxic substances in the fourth revision of Directive 2004/37/EC on the protection of workers from the risks related to exposure to carcinogens or mutagens at work has not yet been reached. The SCCS considers permanent hair dyes safe for consumer use below certain limit concentrations, but notices inconsistent results regarding genotoxicity, and a need for further clarification in in vivo and epidemiological studies.[4] The IARC made a clear distinction regarding the risk of carcinogenicity of hair dyes in hairdressers and consumers classifying hairdressing occupation as probably carcinogenic to humans (Group 2A), while personal use of hair dyes is not classifiable as to its carcinogenicity to humans (Group 3). Clearly, regulatory risk assessment for hair care products should expand to cover also occupational exposures in more detail. Systemizing available data on occupational exposure of hairdressers is another challenge, and recent efforts have been made in this field.[49]

4.3 | Limitations

A limitation of the present systematic review is the small number of identified publications investigating carcinogenic or reproductive adverse effects diagnosed in the period 1995 onwards. Due to a relatively short period in which cases were diagnosed, on the one hand, the absolute numbers of cases with specific adverse outcomes were often small. On the other hand, studies were of overall good methodological and reporting quality with low risk of bias, and for the majority of them important confounding factors were controlled for in statistical analysis, such as age and smoking in cancer studies and in reproductive studies maternal age, habits (smoking, drinking, vitamin use) and medical history of previous pregnancies. Unfortunately, the associations with specific hairdressing tasks which might provide information on the type and magnitude of exposure were rarely reported, which limits the elaboration of best preventive measures. We could thus neither confirm nor exclude that occupational exposure to oxidative hair dyes, bleaching, or waving products contributes significantly to an increased risk for cancer and reproductive effects. As several lines of evidence do show mutagenic effects of chemicals in the hair products, further epidemiological studies are warranted. Furthermore, more detailed information on exposure in these studies would be essential, for example daily or weekly frequencies of hairdressing tasks, exact ingredients in products used in the participating hair salons, measurement of air concentration of chemicals in hair salons or biomonitoring in hairdressers. Our work should therefore be viewed integral with previous monographs (IARC and SCCS opinions), meta-analyses, and systematic reviews of previous epidemiological evidence, as well as available in vivo and in vitro toxicity findings on hairdressing chemicals.

4.4 | Conclusion

Only a minority of recent epidemiological studies in hairdressers found significantly increased risk for carcinogenic effect (bladder cancer) and reprotoxic effects (poor neonatal health indicators and maternal perinatal adverse events). The small number of recent studies included in this review, small number of participants with specific adverse outcomes in the studies, and mostly cross-sectional or case–control study designs must be named as potential limitations of our conclusion. Nevertheless, despite the scarce evidence that hairdressers are at an increased risk of carcinogenic or reprotoxic effects related to their trade, such health risks cannot be completely ruled out. Therefore, preventive efforts to diminish occupational inhalational and skin exposure to hairdressing chemicals should be employed. These could include installation of appropriate ventilation systems alongside the introduction of appropriate ventilation procedures. Also, the importance of existing recommendations for adequate glove use in the everyday working life should be emphasized. Such health-related contents could be conveyed in health education programs. Further, well-designed observational as well as experimental studies on CMR potential of hairdressing products are warranted.

AUTHORS CONTRIBUTION

Ž.B.: investigation, formal analysis, writing – original draft, conceptualization, methodology; M.M., S.H., M. S. H., J.D.J., C.S., W.U., P.W., H.v.d.M., S.K., R.T.:

conceptualization, methodology, writing – review and editing; Z.F.: methodology, writing – original draft; S.M.J., J.M.: conceptualization, methodology, writing – review and editing, supervision.

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DATA AVAILABILITY STATEMENT

The data that support the findings of this review study were derived from the references available in the public domains: databases MEDLINE, Web of Science - core collection, and Cochrane Library, in addition to Scientific Committee on Consumer Safety (SCCS) opinions, and toxicological dossiers of the German Committee for the determination of occupational exposure limits ('MAK-Commission'). All included references are listed in the article and described in detail in Results section.

DISCLOSURE

Ethics statement: As this work was a systematic review of published primary studies, no approval from an ethical review board was required. *Informed consent*: Not applicable, as this work was a systematic review of published primary studies. *Registry and the Registration No. of the study/Trial*: N/A. *Animal studies*: N/A. *Conflict of interest*: W. Uter has received an honorarium for a lecture on contact allergy from mixed dermatopharmaceutical sponsors (GEIDAC, Toledo, Sepember 2018) and travel reimbursement for participation in study meetings of the IDEA project (IFRA). W. Uter is external expert for the SCCS. Other authors declare no conflict of interests for this article.

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APPENDIX 1

Full search string used during systematic literature search

The substance and product type identifiers:

(hairdress*)

OR

(hair dyeing) OR (hair coloring) OR (p-Phenylenediamine) OR (PPD) OR (1,4-Benzenediamine) OR ((4-Aminophenyl)amine) OR (1,4-Diaminobenzene) OR (1,4-Phenylenediamine) OR (4-Aminoaniline) OR (4-Phenylenediamine) OR (C.I. 76060) OR (C.I. Developer 13) OR (C.I. Oxidation Base 10) OR (Paramine) OR (p-Aminoaniline) OR (p-Benzenediamine) OR (p-Diaminobenzene) OR (106-50-3) OR (624-18-0) OR (p-Phenylenediamine sulfate) OR (16245-77-5) OR (Toluene-2,5-diamine) OR (1,4-Benzenediamine, 2-methyl-) OR (2-Methyl-1,4-benzenediamine) OR (1,4-Diamino-2-methylbenzene) OR (1-Methyl-2,5-diam inobenzene) OR (2,5-Diaminotoluene) OR (2,5-Diam inotoluol) OR (2-Methyl-1,4-phenylenediamine) OR (2-Methyl-p-phenylenediamine) OR (4-Amino-2-methyla niline) OR (4-Amino-3-methylaniline) OR (C.I. 76042) OR (Toluylene-2,5-diamine) OR (p-Toluenediamine) OR (95-70-5) OR (Toluene-2,5-diamine sulfate) OR (615-50-9) OR (2-Methoxymethyl-p-phenylenediamine) OR (337906-36-2) OR (2-Methoxymethyl-PPD) OR (1,4-Benzenediamine, 2-(methoxymethyl)) OR (1,4-Benze nediamine, 2-(methoxymethyl)-, sulfate) OR (337906-37-3) OR (2-(Methoxymethyl)-1,4-benzenediamine) OR (1,4-Diamino-2-(methoxymethyl)benzene) OR (2-Metho xymethyl-1,4-benzenediamine) OR (2-Methoxymethyl-1, 4-diaminobenzene) OR (2-Methoxymethyl-1,4-phenylen ediamine)

OR

(persulfate*) OR (persulphate*) OR (Ammonium persulfate) OR (7727-54-0) OR (Peroxydisulfuric acid ([(HO)S(O)_2]_2O_2), diammonium salt (8CI,9CI))) OR (Ammonium peroxidodisulfate) OR (Ammonium peroxydisulfate) OR (Ammonium peroxydisulfate (NH_4)_2S_2O_8)) OR (Ammonium peroxysulfate) OR (Bis(ammonium) peroxodisulfate) OR (Diammonium peroxydisulfate) OR (Diammonium peroxydisulphate) OR (Diammonium persulfate) OR (Potassium persul-fate) OR (7727-21-1) OR (Peroxydisulfuric acid ([(HO) S(O)_2]_2O_2), dipotassium salt (9CI)) OR (Dipotassium peroxodisulfate) OR (Dipotassium peroxydisulfate) OR (Dipotassium persulfate) OR (Potassium dipersul-fate) OR (Potassium peroxydisulfate) OR (Potassium peroxydisulfate (K_2(S_2O_8))) OR (Potassium peroxydisulphate) OR (Sodium persulfate) OR (7775-27-1) OR (Peroxydisulfuric acid ([(HO)S(O)_2]_2O_2), disodium salt (8CI,9CI))) OR (Sodium peroxydisulfate (6CI)) OR (Disodium peroxodisulfate) OR (Disodium peroxydisulfate) OR (Disodium persulfate) OR (Sodium dipersulfate) OR (Sodium peroxodisulfate) OR (Sodium peroxydisulfate (Na_2S_2O_8)) OR (Sodium persulfate (Na_2S_2O_8))

OR

(acid perm) OR (permanent wave) OR (glyceryl thio-glycolate) OR (glyceryl monothioglycolate) OR (30618-84-9) OR (Acetic acid, mercapto-, ester with glycerol (6CI)) OR (Acetic acid, mercapto-, monoester with 1,2,3-propanetriol (9CI)) OR (Acetic acid, mercapto-, monoester with glycerol (8CI)) OR (Glycerol monomer-captoacetate) OR (Ammonium thioglycolate) OR (5421-46-5) OR (Acetic acid, mercapto-, monoammonium salt (8CI,9CI)) OR (Ammonium mercaptoacetate) OR (Ammonium thioglycollate) OR (Thioglycolic acid am-monium salt)

The substance identifiers were combined with outcome identifiers using AND operator.

The outcome identifiers:

Allergens[MeSH] OR Irritants[MeSH] OR allergic OR irritative OR Respiration Disorders[MeSH] OR respiratory OR Inhalation[MeSH] OR Rhinitis[MeSH] OR Asthma

OR Neoplasms[MeSH] OR cancer OR Carcinogens[MeSH] OR Biomarkers, Tumor[MeSH] OR Carcinogenicity Tests[MeSH] OR Mutagens[MeSH] OR Mutagenicity Tests[MeSH] OR genotoxicity

OR

Reproductive Health[MeSH] OR reproductive tox-icity OR reprotoxic OR Pregnancy Outcomes[MeSH] OR Pregnancy Complications[MeSH] OR Pregnancy[MeSH] OR Infertility[MeSH] OR Congenital Abnormalities[MeSH] OR birth defect OR congeni-tal malformations OR Abortion, Spontaneous[MeSH] OR Developmental Disabilities[MeSH] OR develop-mental toxicity OR Menstruation Disturbances[MeSH] OR Spermatogenesis[MeSH] OR Fertility[MESH] OR Fecundability OR Time to pregnancy OR low birth weight

OR

Endocrine Disruptors[MeSH] OR Endocrine System Diseases[MeSH]

ORToxicity Tests[MeSH] OR Toxicity Tests, Acute[MeSH] OR Toxicity Tests, Subacute[MeSH] OR Toxicity Tests, Chronic[MeSH] OR Toxicity Tests, Subchronic OR dermal absorption OR Occupational Diseases[MeSH] OR work related OR hairdresser* OR hairdressing

APPENDIX 2

Criteria for the evaluation of quality and risk of bias for the systematic reviews addressing health effects of hair cosmetic ingredients

References1. Pluye P, Gagnon M-P, Griffiths F, Johnson-Lafleur J. A scoring system for appraising mixed methods research, and concomitantly appraising qualitative, quantitative and mixed methods primary studies in Mixed Studies Reviews. Int J Nurs Stud. April 2009;46(4):529–46.

2. Sterne JAC, Hernán MA, McAlleenan A, Reeves BC, Higgins JPT. Chapter 25: Assessing risk of bias in a non-randomized study. In: Cochrane Handbook for Systematic Reviews of Interventions. 6.1. 2020.

3. Anon. A Summary of General Assessment Factors for Evaluating the Quality of Scientific and Technical Information - Prepared for the U.S. Environmental Protection Agency by members of the Assessment Factors Workgroup, a group of the EPA's Science Policy Council. Washington, DC: US EPA; 2003.

"AD: Appropriate design, sampling and sample" (1+2+3)

AD1: Appropriate, scientifically based study design	"yes": *Study design is fit for the objectives of the study*	**AD1:** 1
	"unclear or no"	0
AD2: Appropriate sample size	"adequate	**AD2:** 1
	"partly"	0.5
	"no"	0
AD3: Appropriate sample description	"Full": *age (range or mean or median or anything), gender distribution, time period tested, drop-out*;	**AD3:** 2
	"Partial": *any omission from above*	1
	"No"	0
AD4: Selection bias	"No indication of differential selection of patients/participants into the study" *In clinical, patient-based studies, no indication of selection (other than inevitable one owing to health care system) in terms of inclusion and missing data. In epidemiological studies: appropriate sampling strategy, no indication of selective participation or loss to follow-up*.	**AD4:** 1
	"Clear indication of above"	0
AD5: Information bias	"No indication of exposure and/or outcome-related misclassification" *In clinical, patient-based studies, no indication of an effect of group (*e.g. *being hairdresser or not) on outcome reading, and* vice versa.	**AD5:** 1
	"Clear indication of above"	0
AD6: Funder/sponsoring documented	"Fully/adequately": *In studies based on routine clinical data (patient-based) institutional affiliation and a conflict of interest statement is given*	**AD6:** 1
	"Partly": no CoI statement or no institutions given	0.5
	"no": both lacking	0

"JM: Justification of methodology (validity and standards)" (1 + 3)

JM1: Appropriate, scientifically based methodology	"Yes"	**JM1:** 1
	"Unclear or no"	0
JM2: Adequate use and description of methods	"Full"	**JM2:** 2
	"Partial"	1
	"Unclear or no"	0
JM3: Validation/standardization of used methods	"Yes"	**JM3:** 1
	"Partial"	0.5
	"No or unclear"	0

"JR: Justification/presentation of results" (1 + 3)

JR1: Results clearly and completely documented	"Fully/adequately"	**JR1:** 1
	"Partly"	0.5
	"No or unclear"	0
JR2: Appropriate statistical techniques	"Fully/adequately": *In descriptive statistics, provision of confidence intervals; when using statistical inference, appropriate statistical tests need to be employed. Analytical techniques such as multifactorial analyses need to be evaluated on a case-by-case basis*	**JR2:** 1
	"Partly": *no confidence limits*	0.5
	"Unclear or no": *wrong statistical tests employed*	0
JR3: All measurements mentioned in the methods are reported	"Yes"	**JR3:** 1
	"No"	0
JR4: Independent peer review	"Yes": if published in a peer-reviewed scientific journal	**JR4:** 1
	"Unclear or no": otherwise	0