# **Systematic Reviews and Meta- and Pooled Analyses**

# Lung Cancer Risk Among Hairdressers: A Pooled Analysis of Case-Control Studies Conducted Between 1985 and 2010

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Initially submitted January 11, 2013; accepted for publication May 21, 2013.

Increased lung cancer risks among hairdressers were observed in large registry-based cohort studies from Scandinavia, but these studies could not adjust for smoking. Our objective was to evaluate the lung cancer risk among hairdressers while adjusting for smoking and other confounders in a pooled database of 16 case-control studies conducted in Europe, Canada, China, and New Zealand between 1985 and 2010 (the Pooled Analysis of Case-Control Studies on the Joint Effects of Occupational Carcinogens in the Development of Lung Cancer). Lifetime occupational and smoking information was collected through interviews with 19,369 cases of lung cancer and 23,674 matched population or hospital controls. Overall, 170 cases and 167 controls had ever worked as hairdresser or barber. The odds ratios for lung cancer in women were 1.65 (95% confidence interval (CI): 1.16, 2.35) without adjustment for smoking and 1.12 (95% CI: 0.75, 1.68) with adjustment for smoking; however, women employed before 1954 also experienced an increased lung cancer risk after adjustment for smoking (odds ratio = 2.66, 95% CI: 1.09, 6.47). The odds ratios in male hairdressers/barbers were generally not elevated, except for an increased odds ratio for adenocarcinoma in long-term barbers (odds ratio = 2.20, 95% CI: 1.02, 4.77). Our results suggest that the increased lung cancer risks among hairdressers are due to their smoking behavior; single elevated risk estimates should be interpreted with caution and need replication in other studies.

case-control studies; hair bleaching agents; hair color; lung neoplasms; occupational exposure

Abbreviations: AUT-Munich, Arbeit und Technik-Munich; CI, confidence interval; LUCAS, Lungcancer i Stockholm; MORGEN, Monitoring van Risicofactoren en Gezondheid in Nederland; SYNERGY, Pooled Analysis of Case-Control Studies on the Joint Effects of Occupational Carcinogens in the Development of Lung Cancer.

The World Health Organization's International Agency for Research on Cancer classified "occupational exposures of hair-dressers and barbers" as probably carcinogenic to humans (Group 2A) in 1993 and 2010 on the basis of limited evidence

for an association with bladder cancer, mainly in men (1, 2). Increases in lung cancer risk (20%-40%) have been observed in several cohort studies and a few case-control studies (3). Nevertheless, the evidence for an association between

occupation as hairdresser or barber and lung cancer is not conclusive because most of the data from cohort studies come from linkage between census data and cancer registry data, primarily in the Scandinavian countries, which provide excellent opportunities to monitor cancer risks by occupation but offer limited ability to control for tobacco smoking and other confounders (4). The case-control studies have not been convincing because of lack of power and details about type, calendar period, and duration of employment as a hairdresser (5, 6).

Hairdressers and barbers can be exposed to a wide range of chemicals, such as volatile organic chemicals (e.g., toluene, ethanol, isopropanol, ether, diaminotoluene, phenylenediamine) via hairsprays and setting lotions, as well as ammonia, ammonium persulfates, hydrogen peroxide, and organic pigments as ingredients of permanent waves, hair dyes, and hair bleaching applications (7, 8). Important changes in the composition and use of hair products have taken place over the years; many hazardous dyes have been phased out, and chlorinated solvents used as propellants in hair sprays (e.g., methylene chloride) have been replaced by less harmful organic solvents (9). Work-related skin and respiratory symptoms remain frequent, and together with musculoskeletal complaints, contribute to many hairdressers leaving their jobs within a few years of starting to work as hairdressers (10). Products used by hairdressers are used on their customers. If some of the products were carcinogenic, this would have implications for the general public. Some studies have indeed suggested an increased risk of cancer from personal use of hair dyes, but the overall evidence was not conclusive (1, 2). Occupational studies typically involve stronger exposure contrasts and might therefore provide better options to investigate a cancer risk, which in turn might also inform about carcinogenic hazards of consumer products. Pooling communitybased case-control studies appears to be the best available alternative to explore why hairdressers experience an increased lung cancer risk, especially because they often work only a few years as hairdressers and because of availability of information on life-long smoking habits. The Pooled Analysis of Case-Control Studies on the Joint Effects of Occupational Carcinogens in the Development of Lung Cancer (SYNERGY) project is the largest data set of its kind with complete smoking and occupational information.

Our objective was to study the potential association between employment as a hairdresser and increased lung cancer risk in SYNERGY, while adjusting for tobacco smoking. We stratified analyses by sex, type of hairdresser, calendar period of employment, and lung cancer histology. We also compared smoking habits between hairdressers and nonhairdressers.

#### **MATERIALS AND METHODS**

## Study population and data collection

The SYNERGY project includes data from 16 case-control studies on lung cancer conducted in 13 European countries, Canada, New Zealand, and China between 1985 and 2010. The Lungcancer i Stockholm (LUCAS) Study, a study of lung cancer in France, and a case-control study of male lung cancer, occupational exposures, and smoking in Hong Kong were restricted to men, and the lung cancer study in Paris included only former and current smokers. The International Agency for Research on Cancer Multicenter Case-Control Study of Occupation, Environment, and Lung Cancer in Central and Eastern Europe (INCO-COPERNICUS) is a multicenter study in Central and Eastern Europe and includes participants from the Liverpool Lung Project in the United Kingdom (11). The 7 countries in that study are participating as separate studies in SYNERGY. Monitoring van Risicofactoren en Gezondheid in Nederland (MORGEN) is a case-control study nested in the prospective European Prospective Investigation Into Cancer and Nutrition (EPIC) cohort in the Netherlands, and the study participants filled in a questionnaire at recruitment (12). Besides MORGEN, all studies have provided data on lifetime smoking habits and complete occupational history. Cases were recruited from hospitals or cancer registries, and the case definition varied slightly across the original studies. In most studies, cases were eligible if they: 1) were younger than 75 years; 2) had been a resident of the study area for at least 1 year, and 3) had a final diagnosis of lung cancer confirmed by histology or cytology. Controls were recruited from the general population (81%) or hospitals (19%) and were individually matched or frequency matched to cases by sex and age (±3 years). Information was collected predominantly by interviews with the subjects themselves, though next-of-kin respondents were accepted in LUCAS (Sweden), Investigations Cancers Respiratoires et Environnement (ICARE; France), a case-control study of environmental causes of lung cancer in Montreal, Canada, the study in Hong Kong (China), and Occupational Cancer in New Zealand (OCANZ; New Zealand) if subjects were unavailable (9.1% of cases, 6.6% of controls). In most studies, face-to-face interviews (87% of study population) were conducted; however, in LUCAS and MORGEN, questionnaires were sent via mail, and in the study in Hong Kong, the study in Montreal, a lung cancer case-control study in Toronto, Canada, and OCANZ, parts of the study populations were interviewed via telephone. More information about the SYNERGY project is available at http://synergy. iarc.fr/ and in previously published papers (13-15). The subtype of lung cancer was classified according to World Health Organization guidelines by pathologists associated with the participating hospitals. Reference pathology was performed for the German cases (16). For the original studies, ethics approval was obtained in accordance with legislation in each country. In addition, for the pooling project, ethics approval was obtained from the International Agency for Research on Cancer Ethics Committee, and therefore the project has been conducted in accordance with the ethics standards in the 1964 Declaration of Helsinki and subsequent amendments.

#### Identification of hairdressers and barbers

The occupational data was coded or recoded to the International Standard Classification of Occupations issued by International Labour Office in 1968 (17). We studied all hairdressers (International Standard Classification of Occupations: 5-70.20 and 5-70.30), as well as women's hairdressers (International Standard Classification of Occupations: 5-70.20) and barbers (International Standard Classification of Occupations: 5-70.30) separately. Women's hairdressers cut

Table 1. Description of the Studies Included in the SYNERGY Project, 1985–2010

First Author, Year	Study (Short		Data	C	ases	Co	ontrols	Source of	Data	
(Reference No.)	Names)	Country	Collection Period	No.	Response Rate, %	No.	Response Rate, %	Controls	Source	Interviewee
Bruske-Hohlfeld, 2000 (23)	AUT-Munich	Germany	1990–1995	3,180	77	3,249	41	Р	I	S
Jöckel, 1998 (24)	HdA	Germany	1988–1993	1,004	69	1,004	68	Р	1	S
Consonni, 2010 (25)	EAGLE	Italy	2002-2005	1,943	87	2,116	72	Р	1	S
Richiardi, 2004 (26)	TURIN/VENETO	Italy	1990-1994	1,132	79	1,553	80	Р	1	S
Fortes, 2003 (27)	ROME	Italy	1993-1996	347	74	365	63	Н	1	S
Stücker, 2002 (28)	LUCA	France	1989-1992	309	98	302	98	Н	1	S
Kazma, 2012 (29)	PARIS	France	1988–1992	173	95	234	95	Н	1	S
Guida, 2011 (30)	ICARE	France	2001-2007	2,926	87	3,555	81	Р	1	S and NOK
Lopez-Cima, 2007 (31)	CAPUA	Spain	2000–2010	875	91	838	96	Н	1	S
Riboli, 1997 (12)	MORGEN <sup>a</sup>	Netherlands	1993–1997	71	N/A	202	N/A	Р	Q	S
Scelo, 2004 (32)	INCO	Czech Republic	1999–2002	304	94	453	80	Н	1	S
Scelo, 2004 (32)	INCO	Hungary	1998-2001	402	90	315	100	Н	1	S
Scelo, 2004 (32)	INCO	Poland	1998-2002	800	88	841	88	P and H	1	S
Scelo, 2004 (32)	INCO	Slovakia	1998-2002	346	90	285	84	Н	1	S
Scelo, 2004 (32)	INCO	Romania	1998-2002	181	90	228	99	Н	1	S
Scelo, 2004 (32)	INCO	Russia	1998-2001	600	96	580	90	Н	1	S
Scelo, 2004 (32)	INCO-LLP	United Kingdom	1998-2005	442	78	918	84	Р	1	S
Gustavsson, 2000 (33)	LUCAS	Sweden	1985-1990	1,042	87	2,356	85	Р	Q	S and NOK
Corbin, 2011 (34)	OCANZ	New Zealand	2003-2009	457	53	792	48	Р	I and T	S and NOK
Ramanakumar, 2007 (35)	MONTREAL	Canada	1996-2002	1,203	85	1,509	69	Р	I and T	S and NOK
Brenner, 2012 (36)	TORONTO	Canada	1997–2002	425	62	910	71	P and H	I and T	S
Tse, 2012 (37)	HONG KONG	China	2003-2007	1,207	96	1,069	48	Р	I and T	S and NOK
Overall			1985–2010	19,369	82	23,674	67			

Abbreviations: AUT-Munich, Arbeit und Technik-Munich; CAPUA, Cancer de Pulmon en Asturias; EAGLE, Environment and Genetics in Lung Cancer Etiology; H, control subjects enrolled from hospitals; HdA, Humanisierung des Arbeitslebens; HONG KONG, male lung cancer, occupational exposures, and smoking—a case-control study in Hong Kong; I, face-to-face interview; ICARE, Investigations Cancers Respiratoires et Environnement; INCO, International Agency for Research on Cancer Multicenter Case-Control Study of Occupation, Environment, and Lung Cancer in Central and Eastern Europe; LLP, Liverpool Lung Project; LUCA, study of lung cancer in France; LUCAS, Lungcancer i Stockholm; MONTREAL, Montreal case-control study of environmental causes of lung cancer; MORGEN, Monitoring van Risicofactoren en Gezondheid in Nederland; N/A, not applicable; NOK, next-of-kin, for example, husband or wife of the study participant; OCANZ, Occupational Cancer in New Zealand; P, control subjects enrolled from the general population; PARIS, lung cancer study in Paris; Q, self-administered questionnaire; ROME, Rome lung cancer case-control study; S, study participant; T, over-the-phone interview; TORONTO, Toronto lung cancer (case-control) study; TURIN/VENETO, population-based case-control study of lung cancer in the city of Turin and in the Eastern part of Veneto Region.

<sup>&</sup>lt;sup>a</sup> Nested case-control study.

Table 2. General Characteristics of Hairdressers/Barbers and Nonhairdressers/Nonbarbers in the SYNERGY Project, 1985–2010

		Hairdr	essers			Nonhai	rdressers	
Characteristics	Ca	ises	Con	ntrols	Case	es	Con	trols
	No.	%	No.	%	No.	%	No.	%
Men								
Total	100		107		15,095		18,109	
Age, years	64.7	(8.3) <sup>a</sup>	64.0	(8.9) <sup>a</sup>	62.7 (9	0.0) <sup>a</sup>	62.2 (9	.5) <sup>a</sup>
≤40	1	1.0	1	0.9	200	1.3	398	2.2
41–50	4	4.0	7	6.5	1,362	9.0	1,857	10.2
51–60	19	19.0	26	24.3	4,106	27.2	4,698	25.9
61–70	52	52.0	46	43.0	6,206	41.1	7,373	40.7
71–80	23	23.0	25	23.4	3,165	21.0	3,736	20.6
>80	1	1.0	2	1.9	56	0.4	47	0.3
Smoking status								
Never	4	4.0	24	22.4	464	3.1	4,707	26.0
Former	28	28.0	49	45.8	4,887	32.4	7,925	43.8
Current	68	68.0	34	31.8	9,742	64.5	5,473	30.2
Pack-years of cigarette smoking <sup>b</sup>	48.8	(31.0) <sup>a</sup>	32.0	(26.5) <sup>a</sup>	43.8 (2	(8.2) <sup>a</sup>	27.4 (2	4.3) <sup>a</sup>
Time since quitting smoking	5.0	(9.5) <sup>a</sup>	11.1 (	(12.9) <sup>a</sup>	5.2 (9	.1) <sup>a</sup>	11.7 (1	3.6) <sup>a</sup>
Current smoker	68	68.0	34	31.8	9,742	64.5	5,473	30.2
Former smoker								
2-7 years	10	10.0	10	9.4	1,641	10.9	1,170	6.5
8-15 years	7	7.0	9	8.4	1,470	9.7	1,809	10.0
16-25 years	6	6.0	17	15.9	1,091	7.2	2,220	12.3
≥26 years	5	5.0	12	11.2	609	4.0	2,441	13.5
Never smoker	4	4.0	24	22.4	464	3.1	4,707	26.0
List A								
Ever	9	9.0	4	3.7	2,130	14.1	1,663	9.2

**Table continues** 

and dress primarily women's hair or can serve mixed customers, including men and children. Barbers cut and dress the hair of men and shave or trim their beards. Thirteen participants had worked as both women's hairdressers and barbers and therefore contributed to both subanalyses.

### Statistical analysis

Differences in mean lifetime smoking consumption (log pack-years) between hairdressers and nonhairdressers among ever-smoking control subjects were evaluated with the t test. The Pearson  $\chi^2$  test was used to compare the distributions in hairdressers versus nonhairdressers with regard to smoking status and ever having been employed in a job with known lung cancer risk. Odds ratios and 95% confidence intervals of lung cancer risk were estimated with unconditional logistic regression. We stratified analyses by sex, types of hairdressers, and calendar period of employment. We divided the period into 2 segments and chose the cutpoint at the median start of first employment as hairdresser/barber in our study population (1954) to ensure a sufficient number of persons in each

category. With regard to histology, we first included all lung cancers (including all cell types, unknown cell type, and mixed cell types). We thereafter looked at each of the major cell types separately, using the same controls and excluding all cases with another or unknown or mixed cell type. Duration of employment was studied in categories, with tertiles based on the distribution of employment duration of all hairdressers in the control population. Subjects who had never worked as a hairdresser or barber comprised the reference group. P for trend was calculated with the maximum likelihood estimates based on the categorical variables. Odds ratios were adjusted for potential confounders in a stepwise manner: Odds ratio 1 was adjusted for log(age) and study (22 study centers). Odds ratio 2 was further adjusted for smoking in pack-years (log(cigarette pack-years + 1)) as a continuous variable and time since quitting smoking all types of tobacco as a categorical variable (current smokers; former smokers who stopped smoking 2–7 years, 8–15 years, 16–25 years, or  $\geq$ 26 years before interview or diagnosis; or never smokers). Odds ratio 3 was additionally adjusted for ever employment in a job with known lung cancer risk (list A), as a proxy for exposure

Table 2. Continued

		Hairdr	essers			Nonhai	rdressers	
Characteristics	Ca	ises	Cor	ntrols	Cas	es	Con	trols
	No.	%	No.	%	No.	%	No.	%
Women								
Total	70		60		3,585		5,000	
Age, years	56.7	(11.2) <sup>a</sup>	55.1	(10.5) <sup>a</sup>	60.6 (1	0.1) <sup>a</sup>	60.3 (1	1.2) <sup>a</sup>
≤40	7	10.0	3	5.0	99	2.8	266	5.3
41–50	15	21.4	19	31.7	543	15.2	699	14.0
51–60	19	27.1	20	33.3	1,043	29.1	1,319	26.4
61–70	24	34.3	15	25.0	1,227	34.2	1,733	34.7
71–80	5	7.1	2	3.3	653	18.2	969	19.4
>80			1	1.7	20	0.6	14	0.3
Smoking status								
Never	8	11.4	21	35.0	961	26.8	2,997	59.9
Former	14	20.0	18	30.0	680	19.0	1,019	20.4
Current	48	68.6	21	35.0	1,944	54.2	979	19.6
Pack-years of cigarette smoking <sup>b</sup>	33.9	(22.4) <sup>a</sup>	22.1	(22.4) <sup>a</sup>	34.5 (2	(3.0) <sup>a</sup>	19.3 (1	8.3) <sup>a</sup>
Time since quitting smoking	2.3	(4.8) <sup>a</sup>	7.2 (	10.9) <sup>a</sup>	3.4 (7	7.7) <sup>a</sup>	6.9 (1	1.7) <sup>a</sup>
Current smoker	48	68.6	21	35.0	1,944	54.2	979	19.6
Former smoker								
2-7 years	6	8.6	3	5.0	246	6.9	194	3.9
8-15 years	5	7.1	5	8.3	202	5.6	231	4.6
16-25 years	3	4.3	5	8.3	143	4.0	281	5.6
≥26 years			3	5.0	80	2.2	277	5.5
Never	8	11.4	21	35.0	961	26.8	2,997	59.9
List A								
Ever	3	4.3	1	1.7	86	2.4	58	1.2

<sup>&</sup>lt;sup>a</sup> Values expressed as mean and standard deviation.

to occupational lung carcinogens. List A is a list of occupations and industries known to present an excess risk of lung cancer, which were identified by Ahrens and Merletti in 1998 (18) and updated by Mirabelli et al. in 2001 (19). Stability of the results was assessed by restricting the analyses to never smokers and by exploring potential heterogeneity with  $I^2$  measuring the variation in risk estimates attributable to heterogeneity between studies, countries, size of the study ( $\pm 1,500$  participants), year of the study (end of data collection  $\pm 1995$ ), and type of controls (population, hospital, or mixed). Statistical analyses were conducted in SAS, version 9.2 (SAS Institute, Inc., Cary, North Carolina) and STATA, version 12.1 (StataCorp LP, College Station, Texas). A P value of  $\leq 0.05$  was considered statistically significant.

#### **RESULTS**

Table 1 describes the studies included in the SYNERGY project. Study participants who did not provide complete

data for calculation of smoking pack-years (519 cases and 398 controls) were excluded. Thus, 18,850 cases and 23,276 controls were included in these analyses.

Table 2 shows the characteristics of hairdressers/barbers and nonhairdressers/nonbarbers by sex. Comparison of hairdressers versus nonhairdressers with a focus on ever-smoking control subjects showed that the mean cumulative smoking consumption (log pack-years) was not statistically different among men (P = 0.21) or women (P = 0.80). However, the frequency distribution across never, former, and current smokers was significantly different between female hairdressers and nonhairdressers (P < 0.001 in controls) but not between male hairdressers/barbers and nonhairdressers/nonbarbers (P = 0.70in controls). The proportion of participants having worked in a job with known lung cancer risk (list A) was <5% among women overall, and no significant difference was observed between hairdressers and nonhairdressers (P = 0.72 in controls). Among men, hairdressers/barbers had less often been employed in a list A job than had nonhairdressers/nonbarbers

<sup>&</sup>lt;sup>b</sup> Among ever smokers only.

(P = 0.05 in controls). Adjustment for list A in the analyses (odds ratio 3) did not influence the results, so only odds ratio 1 and odds ratio 2 are displayed in Table 3.

#### Lung cancer risk among hairdressers

The proportion of men having worked as women's hair-dressers was 0.20% in cases (n = 30) and 0.22% in controls (n = 40), and the proportion of men having worked as barbers was 0.51% in cases (n = 77) and 0.40% in controls (n = 73) (Table 3). We observed no significant increased risk of lung cancer among male hairdressers, either before or after adjustment for smoking. Among barbers, we observed a nonsignificant trend of increasing odds ratios for lung cancer with longer duration of employment, with odds ratios ranging from 0.83 (95% confidence interval (CI): 0.43, 1.61) to 1.62 (95% CI: 0.88, 2.98), with P = 0.32.

Employment as a hairdresser/barber with regard to time of first employment did not reveal a different risk pattern: Odds ratio 2 was 0.92 (95% CI: 0.52, 1.63) before 1954 and 0.95 (95% CI: 0.65, 1.38) in or later than 1954. With regard to histology, long-term barbers (>26 years of employment) had an increased odds ratio for adenocarcinoma, on the basis of 12 cases (odds ratio 2 = 2.20, 95% CI: 1.02, 4.77).

A meta-analysis by study resulted in an overall odds ratio 2 of 0.93 (95% CI: 0.67, 1.28), with an  $I^2$  of 0% and P = 0.90. Further sensitivity analyses among men revealed no significant heterogeneity in risk estimates with regard to country, calendar period of data collection, size of study, or type of control group, and all overall odds ratios remained <1 (data not shown). In never smokers, odds ratio 1 for male hairdressers/barbers was 1.60 (95% CI: 0.53, 4.82), on the basis of 4 cases.

The proportions of women who had ever been employed as hairdressers among cases and controls were 1.89% (n = 69) and 1.17% (n = 59), respectively. Only 1 female case and 1 female control had worked as barbers, so women's hairdressers and barbers were not analyzed separately. A significant increased lung cancer risk among hairdressers was observed (odds ratio 1 = 1.65, 95% CI: 1.16, 2.35), which was reduced and no longer statistically significant when adjusted for smoking (odds ratio 2 = 1.12, 95% CI: 0.75, 1.68). The highest odds ratio was observed among those who had worked <8 years as hairdressers. No trend in relation to duration was observed, with P = 0.71. The risk changed with time period of employment; women who had been employed as hairdressers before 1954 experienced an increased lung cancer risk before and after adjustment for smoking (odds ratio 1 = 3.01, 95% CI: 1.38, 5.59; oddsratio2=2.66,95% CI: 1.09,6.47), whereas women employed as hairdressers in or later than 1954 did not (odds ratio 1 = 1.41, 95% CI: 0.94, 2.12; odds ratio 2 = 0.89, 95% CI: 0.56, 1.40). Table 4 shows lung cancer risk by calendar period, duration of employment, and lung cancer histology. Female hairdressers first employed before 1954 experienced increased risk of all major lung cancer types, and the strongest association was observed for adenocarcinoma (odds ratio 2 = 3.10, 95%CI: 1.14, 8.43). Across all lung cancer types, the elevated risks were restricted to the short-term hairdressers (<8 years).

A meta-analysis by study resulted in an overall odds ratio 2 of 1.13 (95% CI: 0.74, 1.73), with an  $I^2$  of 0% and P = 0.84. The odds ratio 2 for the Arbeit und Technik–Munich (AUT–

Munich) study alone was 3.25 (95% CI: 1.03, 10.23); when AUT-Munich was excluded, the overall odds ratio 2 decreased to 1.07 (95% CI: 0.80, 1.43). Exclusion of AUT-Munich from the analysis of female hairdressers employed before 1954 resulted in an odds ratio 2 of 2.72 (95% CI: 0.93, 8.02) and in an odds ratio 2 of 3.91 (95% CI: 1.22, 12.50) for adenocarcinoma alone. With regard to the calendar period of data collection in the different studies (taking 1995 as cutpoint), we observed an odds ratio 2 of 1.84 (95% CI: 0.85, 3.98) for women enrolled in the earlier studies and an odds ratio 2 of 1.00 (95% CI: 0.63, 1.59) for the more recent studies, with an  $I^2$  of 42% (P = 0.19). When comparing the risk estimates for the different sources of control subjects, we observed an odds ratio 2 of 1.26 (95% CI: 0.82, 1.95) for population-based case-control studies and odds ratios <1 for hospital-based and mixed case-control studies, with an  $I^2$  of 0% (P = 0.64). No heterogeneity was observed with regard to country or study size (data not shown). In never smokers, female hairdressers experienced an odds ratio 1 of 1.33 (95% CI: 0.57, 3.08), on the basis of 8 cases.

#### DISCUSSION

We investigated hairdressers' and barbers' lung cancer risks compared with nonhairdressers/nonbarbers in the SYNERGY population. Our results show the importance of adjusting for the major risk factor of a certain cancer when investigating a presumably less pronounced and less prevalent other potential risk factor and how this can be done efficiently in a pooled data set of independently conducted studies. In our case, an association reported from a large linkage study could no longer be observed.

The odds ratio for women overall (including both time periods) was significantly elevated before adjustment for smoking but not afterward. Female hairdressers were more often smokers than were nonhairdressers, whereas no significant difference in smoking habits was seen between male hairdressers/barbers and nonhairdressers/nonbarbers in this study. In subgroup analyses, our results revealed an increased risk among women with first employment before 1954 and who had worked <8 years as hairdressers but not in women with first employment after 1954 or who had worked long term as hairdressers, and our results revealed no increased risk among men, except for an increased odds ratio for adenocarcinoma in long-term barbers (>26 years).

Strengths of this study include: 1) The study size was large, as is necessary to study a relatively rare occupation in the general population and to stratify the results by sex and type of hairdresser. 2) Most of the original studies were initiated to study occupational risk factors and therefore collected detailed lifetime work histories. 3) Most interviews were conducted face to face with the study participants. 4) We could adjust for smoking, the most important risk factor for lung cancer. Smoking was a confounder, particularly in women. Our adjustment for list A jobs did not reveal a confounding effect, probably because so few hairdressers/barbers worked in list A jobs that overall are more common in men.

All case-control studies can be affected by some degree of recall bias. However, studies in SYNERGY recorded occupational histories but did not solicit direct information

**Table 3.** Lung Cancer Risk Associated With Hairdressing and Duration of Employment Among 18,850 Cases and 23,276 Controls in the SYNERGY Project, 1985–2010

<b>-</b>	Cas	es	Contr	ols	0.04	050/ 01	OR2	050/ 01
Employment	No.	%	No.	%	OR1	95% CI	OR2	95% CI
Men								
All hairdressers <sup>a</sup>								
Never	15,095	99.3	18,019	99.4	1.00		1.00	
Ever	100	0.7	107	0.6	1.04	0.79, 1.37	0.91	0.66, 1.25
<8 years	34	0.2	33	0.2	1.14	0.70, 1.85	0.82	0.48, 1.41
8–26 years	26	0.2	34	0.2	0.83	0.50, 1.39	0.68	0.38, 1.22
>26 years	40	0.3	40	0.2	1.14	0.73, 1.78	1.26	0.74, 2.12
Women's hairdressers <sup>b</sup>								
Never	15,095	99.8	18,109	99.8	1.00		1.00	
Ever	30	0.2	40	0.2	0.84	0.52, 1.35	0.69	0.40, 1.19
<8 years	18	0.1	14	0.1	1.37	0.68, 2.78	1.12	0.50, 2.52
8–26 years	19	0.1	13	0.1	0.77	0.33, 1.81	0.61	0.24, 1.60
>26 years	3	0.0	13	0.1	0.29	0.08, 1.01	0.25	0.06, 0.98
Barber hairdressers <sup>c</sup>								
Never	15,095	99.5	18,109	99.6	1.00		1.00	
Ever	77	0.5	73	0.4	1.17	0.84, 1.61	1.09	0.76, 1.59
<8 years	21	0.1	22	0.1	1.06	0.58, 1.94	0.83	0.43, 1.61
8–26 years	23	0.2	24	0.1	1.05	0.59, 1.87	0.91	0.47, 1.74
>26 years	33	0.2	27	0.2	1.35	0.81, 2.27	1.62	0.88, 2.98
Women								
All hairdressers <sup>a</sup>								
Never	3,585	98.1	5,000	98.8	1.00		1.00	
Ever	70	1.9	60	1.2	1.65	1.16, 2.35	1.12	0.75, 1.68
<8 years	37	1.0	26	0.5	2.07	1.25, 3.46	1.28	0.72, 2.29
8–26 years	15	0.4	20	0.4	1.00	0.51, 1.97	0.93	0.42, 2.02
>26 years	18	0.5	13	0.3	1.96	0.95, 4.03	1.10	0.48, 2.51

Abbreviations: CI, confidence interval; ISCO, International Standard Classification of Occupations 1968; OR1, odds ratio adjusted for age and study; OR2, odds ratio additionally adjusted for cigarette pack-years and time since quitting smoking.

on the use of specific chemicals, which is especially prone to positive recall bias, and no emphasis had been put on employment as barber or hairdresser. Furthermore, no special alert was present in the general population on a possible cancer risk linked to these occupations, which could have induced cancer patients to report them more frequently than controls. Next-of-kin were interviewed instead of the index subject in a few studies, but these represented a small proportion (<10%) of the cases. Recall bias in the smoking history could have resulted in residual confounding when adjustment was made for smoking; however, the smoking-adjusted increased risks in women are unlikely to be due to residual confounding by smoking. Low response rates among control subjects in some studies might have resulted in selection bias if hairdressers were more likely than other control subjects to be nonrespondents. AUT-Munich, with a response rate of 41%

in controls, was the only single study with a significantly elevated odds ratio in female hairdressers. In the pooled data set and in Humanisierung des Arbeitslebens (HdA), another German study, the lung cancer risk was not increased.

A limitation of the present study was the lack of information on determinants of exposure—for example, to which specific agents these groups of hairdressers were exposed and whether protective devices had been used. The SYNERGY data were collected between 1985 and 2010, and the time of working as a hairdresser covered the period from around the 1930s onward. Both the types and the quantities of products used by hairdressers have changed substantially during this time span, and some exposures might have increased in the late 1940s before they were reduced or changed again in the mid-1980s. Among such exposures, worth mentioning are the use of talc (talc products before 1973 could have been contaminated

<sup>&</sup>lt;sup>a</sup> ISCO: 5-70.20 and 5-70.30.

b ISCO: 5-70.20.

c ISCO: 5-70.30.

Lung Cancer Risk Associated With Hairdressing and Duration of Employment by Start of First Employment in Women Overall (n = 8,585) and in Women by Major Lung Cancer Cell Types in the SYNERGY Project, 1985–2010 Fable 4.

<b>Employment as</b>	Controls		All Lung Cancer	ncer		Adenocarcinoma	noma	Sq	lamous Cel	Squamous Cell Carcinoma		Small Cell	Small Cell Carcinoma
Hairdressers <sup>a</sup>	No.	No.	OR2	12 %56	No.	OR2	12 %56	No.	OR2	12 % S6	No.	OR2	95% CI
Never	2,000	3,585	1.00		1,547	1.00		736	1.00		573	1.00	
Ever (≤1953)	6	22	2.66	1.09, 6.47	10	3.10	1.14, 8.43	7	1.80	0.48, 6.73	က	2.51	0.44, 14.33
<8 years	2	15	12.9	2.67, 62.44	9	14.66	2.75, 78.02	Ŋ	14.09	1.63, 121.62	2	50.99	4.63, 561.67
8-26 years	2	4	0.67	0.13, 3.37	-	0.50	0.05, 5.45	0	0.56	0.07, 4.85	-	0.78	0.03, 21.38
>26 years	2	ო	0.56	0.09, 3.48	ဇ	1.46	0.24, 9.07	0			0		
Ever (>1953)	20	48	0.89	0.56, 1.40	16	0.73	0.39, 1.35	6	1.08	0.47, 2.45	13	1.26	0.60, 2.65
<8 years	24	22	0.67	0.35, 1.30	80	0.65	0.28, 1.54	က	0.49	0.13, 1.91	9	1.12	0.40, 3.17
8-26 years	15	7	1.02	0.42, 2.50	9	1.48	0.53, 4.12	-	0.91	0.11, 7.85	က	1.82	0.35, 9.37
>26 years	11	15	1.28	0.51, 3.17	7	0.30	0.06, 1.46	Ŋ	2.92	0.80, 10.65	4	1.23	0.32, 4.77

Abbreviations: CI, confidence interval; ISCO, International Standard Classification of Occupations 1968; OR2, odds ratio adjusted for age, study, cigarette pack-years, and time since quitting smoking.

ISCO 5-70.20 and 5-70.30

by asbestos (20)), propellants, coloring agents, and passive

We observed an increased risk of lung cancer among female hairdressers first employed before 1954, but it was restricted to women working <8 years in this job, and we observed a somewhat higher odds ratio for the earlier studies than for the more recent studies, which could indicate that hairdressers previously experienced an increased risk of lung cancer. This result should, however, be interpreted with caution because the number of hairdressers employed before 1954 was low (22 cases, 9 controls), resulting in wide confidence intervals, and risks were increased only in women with the shortest duration of employment. Also, this hypothesis does not get support from cohort studies. A Finnish study linked census data with cancer registry data for 1970-1987 and found 13 lung cancer cases among female hairdressers, resulting in a standardized incidence ratio of 1.72 (95% CI: 0.92, 2.94). The standardized incidence ratio for lung cancer was below unity for 1970-1981 and was significantly elevated in the later period, 1982-1987 (standardized incidence ratio = 2.92, 95% CI: 1.46, 5.22) (21). A similar study in Sweden investigated hairdressers in 1960-1990 and found an increased risk of lung cancer in both male and female hairdressers, with standardized incidence ratios of 1.38 (95% CI: 1.16, 1.68) and 1.35 (95% CI: 1.15, 1.58), respectively. When they analyzed the earlier period (before 1960) separately, the risk was similar for men (standardized incidence ratio = 1.41, 95% CI: 1.18, 1.68) and somewhat lower (standardized incidence ratio = 1.22, 95% CI: 1.00, 1.47) for female hairdressers (22). However, those results are not directly comparable with the present study, because employment as barbers/hairdressers is often abandoned early and census information refers to the current job, so it is not likely that the employment periods in these cohorts correspond to the employment periods in SYNERGY.

We observed an association in men between long-term employment as a barber and adenocarcinoma, but not squamous cell carcinoma or small cell carcinoma. Interestingly, in the Nordic Occupational Cancer Study (NOCCA), a similar observation was made in the combined Nordic population followed up during 1961-2005. Among male hairdressers, the standardized incidence ratio for all lung cancer types combined was 1.22 (95% CI: 1.12, 1.33), but it was 1.33 (95% CI: 1.10, 1.60) for adenocarcinoma alone. The standardized incidence ratio for all lung cancer types combined in women hairdressers was 1.30 (95% CI: 1.19, 1.42), and it was 1.38 (95% CI: 1.19, 1.61) for adenocarcinoma (4).

Our results in never smokers (slightly elevated nonsignificant odds ratios) were limited by their small numbers.

In summary, our observed association with adenocarcinoma in both men and women is supported by results from the Nordic Occupational Cancer Study, whereas our other findings are not directly comparable with results in the previous literature. Although the statistical power to detect an increased risk was limited in the subanalyses, and our extensive stratification leading to multiple comparisons could have resulted in high variation of the risk estimates and spurious findings by chance, it was important to conduct these analyses because this is a rare opportunity to study hairdressers in a population-based study with detailed smoking information covering such a long calendar period.

Our results suggest that the increased lung cancer risk among female hairdressers is due to smoking behavior among this occupational group and is not directly related to occupational exposure. Single elevated risks among the many subgroup analyses should be interpreted with caution unless replicated in other studies.

#### **ACKNOWLEDGMENTS**

Author affiliations: International Agency for Research on Cancer, Lyon, France (Ann C. Olsson, Yiwen Xu, Joachim Schüz, Jelle Vlaanderen, Kurt Straif); The Institute of Environmental Medicine, Karolinska Institutet, Stockholm, Sweden (Ann C. Olsson, Per Gustavsson, Nils Plato); Institute for Risk Assessment Sciences, Utrecht, the Netherlands (Hans Kromhout, Roel Vermeulen, Susan Peters); Western Australian Institute for Medical Research, Perth, Australia (Susan Peters); L'Institut National de la Santé et de la Recherche Médicale (Inserm), Centre for Research in Epidemiology and Population Health (CESP), U1018, Environmental Epidemiology of Cancer Team, F-94807, Villejuif, France (Isabelle Stücker, Florence Guida); Université Paris-Sud, Unité Mixed de Recherche en Santé (UMRS) 1018, F-94807, Villejuif, France (Isabelle Stücker, Florence Guida); Institut für Epidemiologie I, Deutsches Forschungszentrum fur Gesundheit und Umwelt, Neuherberg, Germany (Irene Brüske, Heinz-Erich Wichmann); Unit of Epidemiology, Fondazione Istituto Di Ricovero e Cura a Carattere Scientifico (IRCCS) CáGranda—Ospedale Maggiore Policlinico, Milan, Italy (Dario Consonni); National Cancer Institute, Bethesda, Maryland (Maria Teresa Landi, Neil Caporaso); Division of Occupational and Environmental Health, School of Public Health and Primary Care, The Chinese University of Hong Kong, Hong Kong, China (Lap Ah Tse, Ignatius Tak-sun Yu); University of Montréal Hospital Research Center (CRCHUM), Montreal, Canada (Jack Siemiatycki, Lesley Richardson); Cancer Epidemiology Unit, Department of Medical Sciences, University of Turin, Turin, Italy (Dario Mirabelli, Lorenzo Richiardi); Department of Environmental Medicine and Public Health, University of Padua, Padua, Italy (Lorenzo Simonato); Institute for Medical Informatics, Biometry and Epidemiology, University of Duisburg-Essen, Essen, Germany (Karl-Heinz Jöckel); Bremen Institute for Prevention Research and Social Medicine, Bremen, Germany (Wolfgang Ahrens, Hermann Pohlabeln); The Biomedical Research Centre Network for Epidemiology and Public Health (CIBERESP), University of Oviedo, Oviedo, Spain (Adonina Tardón); Russian Cancer Research Centre, Moscow, Russia (David Zaridze); Roy Castle Lung Cancer Research Programme, Cancer Research Centre, University of Liverpool, Liverpool, United Kingdom (Michael W. Marcus); Centre for Public Health Research, Massey University, Wellington, New Zealand (Andrea 't Mannetje, Neil Pearce); Occupational Cancer Research Centre, Toronto, Canada (John McLaughlin, Paul Demers); The Nofer Institute of Occupational Medicine, Lodz, Poland (Neonila Szeszenia-Dabrowska); The M Sklodowska-Curie Cancer Center and Institute of Oncology, Warsaw, Poland (Jolanta Lissowska): National Institute of Environment Health, Budapest, Hungary (Peter Rudnai); Regional Authority of Public Health, Banska Bystrica, Slovakia (Eleonora Fabianova); Institute of Public Health, Bucharest, Romania (Rodica Stanescu Dumitru); Institute of Hygiene and Epidemiology, 1st Faculty of Medicine, Charles University, Prague, Czech Republic (Vladimir Bencko); Masaryk Memorial Cancer Institute, Brno, Czech Republic (Lenka Foretova); Palacky University, Faculty of Medicine, Olomouc, Czech Republic (Vladimir Janout); The Tisch Cancer Institute, Mount Sinai School of Medicine, New York, New York (Paolo Boffetta); International Prevention Research Institute, Lyon, France (Paolo Boffetta); Clinical Epidemiology Unit, Istituto Dermopatico dell'Immacolata (IDI)—Istituto di Ricovero e Cura a Carattere Scientifico (IRCCS), Rome, Italy (Christina Fortes); The National Institute for Public Health and Environmental Protection (RIVM), Bilthoven, the Netherlands (Bas Buenode-Mesquita); and Institute for Prevention and Occupational Medicine of the German Social Accident Insurance—Institute of the Ruhr-Universität Bochum (IPA), Bochum, Germany (Benjamin Kendzia, Thomas Behrens, Beate Pesch, Thomas Brüning).

The SYNERGY project is funded by the German Social Accident Insurance (DGUV). The Montreal case-control study of environmental causes of lung cancer was supported by the Canadian Institutes for Health Research and Guzzo-SRC Chair in Environment and Cancer. The Toronto lung cancer case-control study was funded by the National Cancer Institute of Canada with funds provided by the Canadian Cancer Society, and the occupational analysis was conducted by the Occupational Cancer Research Centre, which was supported by the Workplace Safety and Insurance Board, the Canadian Cancer Society, and Cancer Care Ontario. The Investigations Cancers Respiratoires et Environnement (ICARE) study was supported by the French Agency of Health Security (ANSES), the Fondation de France, the French National Research Agency (ANR), the National Institute of Cancer (INCA), the Fondation for Medical Research (FRM), The French Institute for Public Health Surveillance (InVS), The Health Ministry (DGS), the Organization for the Research on Cancer (ARC), and the French Ministry of work, solidarity, and public function (DGT). The lung cancer in France study was supported by the Fondation de France. The lung cancer study in Paris was funded by Organization for the Research on Cancer. The Arbeit und Technik (AUT) study in Germany was funded by the Federal Ministry of Education, Science, Research, and Technology (grant 01 HK 173/0). The Humanisierung des Arbeitslebens (HdA) study was funded by the Federal Ministry of Science (grant 01 HK 546/8) and the Ministry of Labour and Social Affairs (grant IIIb7-27/13). The International Agency for Research on Cancer Multicenter Case-Control Study of Occupation, Environment, and Lung Cancer in Central and Eastern Europe and the United Kingdom (INCO) study was supported by a grant from the European Commission's INCO-Copernicus program (contract IC15-CT96-0313). In Warsaw, the study was supported by a grant from the Polish State Committee for Scientific Research (grant SPUB-M-COPERNICUS/P-05/ DZ-30/99/2000). In Liverpool, the work was funded by the Roy Castle Foundation as part of the Liverpool Lung Project. The Environment and Genetics in Lung Cancer Etiology (EAGLE) study was funded by the Intramural Research Program of the National Institutes of Health, National Cancer Institute,

Division of Cancer Epidemiology and Genetics, Bethesda, Maryland; the Environmental Epidemiology Program of the Lombardy Region, Italy; and the Istituto Nazionale per l'Assicurazione contro gli Infortuni sul Lavoro, Rome, Italy. The Turin/Veneto study (apopulation-based case-control study of lung cancer in the city of Turin and in the Eastern part of Veneto Region) was supported by the Italian Association for Cancer Research, Region Piedmont, Compagnia di San Paolo. The study in Rome was conducted with partial support from the European Union Nuclear Fission Safety Program (grant F14P-CT96-0055) and from the Lazio Region. The Monitoring van Risicofactoren en Gezondheid in Nederland (MORGEN) study was supported by the Dutch Ministry of Health, Welfare and Sports, National Institute of Public Health and the Environment, and the Europe Against Cancer Program. The Cancer de Pulmon en Asturias (CAPUA) study was supported by the Instituto Universitario de Oncologia, Universidad de Oviedo, Asturias, the Fondo de Investigación Sanitaria (FIS) and the Ciber de Epidemiologia y Salud Publica (CIBER-ESP), Spain. The Lungcancer i Stockholm (LUCAS) study was supported by the Swedish Council for Work Life Research and the Swedish Environmental Protection Agency. The study in Hong Kong was supported by a grant from the Research Grants Council of the Hong Kong Special Administrative Region, China (project CUHK4460/03M). The Occupational Cancer in New Zealand (OCANZ) study was funded by the Health Research Council of New Zealand, the New Zealand Department of Labour, Lottery Health Research, and by the Cancer Society of New Zealand.

We thank Veronique Luzon at the International Agency for Research on Cancer for pooling and managing the data.

Preliminary results have been presented as posters at 2 international conferences: the American Association for Cancer Research 102nd Annual Meeting, April 2–6, 2011, in Orlando, Florida, and the 22nd International Conference on Epidemiology in Occupational Health, September 6–9, 2011, in Oxford, United Kingdom. Preliminary results have also been presented in a Master thesis by Yiwen Xu for a Degree of Master of Medical Science with a Major in Public Health Sciences at Karolinska Institutet, Stockholm, Sweden, in 2012.

Conflict of interest: None.

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