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Bigert, Carolina MD, PhD; Gustavsson, Per MD, PhD; Straif, Kurt MD, PhD; Pesch, Beate PhD; Bruning, Thomas MD, PhD; Kendzia, Benjamin MSc; Schuz, Joachim PhD; Stucker, Isabelle PhD; Guida, Florence PharmD; Bruske, Irene MD; Wichmann, Heinz-Erich PhD; Pesatori, Angela C. MD, PhD; Landi, Maria Teresa MD, PhD; Caporaso, Neil MD; Tse, Lap Ah PhD; Yu, Ignatius Tak-sun PhD; Siemiatycki, Jack PhD; Pintos, Javier PhD; Merletti, Franco PhD; Mirabelli, Dario MD; Simonato, Lorenzo MD; Jockel, Karl-Heinz PhD; Ahrens, Wolfgang PhD; Pohlabeln, Hermann PhD; Tardon, Adonina PhD; Zaridze, David MD, PhD; Field, John PhD; 't Mannetje, Andrea PhD; Pearce, Neil PhD; McLaughlin, John PhD; Demers, Paul PhD; Szeszenia-Dabrowska, Neonila PhD; Lissowska, Jolanta PhD; Rudnai, Peter PhD; Fabianova, Eleonora MD, PhD; Stanescu Dumitru, Rodica PhD; Bencko, Vladimir MD, PhD; Foretova, Lenka MD, PhD; Janout, Vladimir PhD; Boffetta, Paolo MD, MPH; Forastiere, Francesco MD; Bueno-de-Mesquita, Bas MD, MPH; Peters, Susan PhD; Vermeulen, Roel PhD; Kromhout, Hans PhD; Olsson, Ann C. PhD

Informazioni sull'Autore

From the Institute of Environmental Medicine (Drs Bigert and Gustavsson), Karolinska Institutet, Stockholm, Sweden; International Agency for Research on Cancer (Drs Straif, Schuz, and Olsson), Lyon, France; Institute for Prevention and Occupational Medicine of the German Social Accident Insurance-Institute of the Ruhr-Universitat Bochum (IPA) (Drs Pesch and Bruning, Mr Kendzia), Germany; Inserm, Centre for Research in Epidemiology and Population Health (CESP) (Drs Stucker and Guida), U1018, Environmental Epidemiology of Cancer Team, F-94807, Villejuif, France; Universite Paris-Sud (Drs Stucker and Guida), UMRS 1018, F-94807, Villejuif, France; Institut fur Epidemiologie I (Drs Bruske and Wichmann), Deutsches Forschungszentrum fur Gesundheit und Umwelt, Neuherberg, Germany; Department of Clinical Sciences and Community Health (Dr Pesatori), Universita degli Studi di Milano, Milan, Italy; National Cancer Institute (Drs Landi and Caporaso), Bethesda, MD; Division of Occupational and Environmental Health (Drs Tse and Yu), School of Public Health and Primary Care, The Chinese University of Hong Kong, China; Research Centre of University of Montreal Hospital Centre (Drs Siemiatycki and Pintos), University of Montreal, Canada; Cancer Epidemiology Unit (Drs Merletti and Mirabelli), Department of

Medical Sciences, University of Turin, Italy; Department of Environmental Medicine and Public Health (Dr Simonato), University of Padua, Italy; Institute for Medical Informatics (Dr Jockel), Biometry and Epidemiology, University of Duisburg-Essen, Essen, Germany; Bremen Institute for Prevention Research and Social Medicine (Drs Ahrens and Pohlabeln), Bremen, Germany; CIBERESP (Dr Tardon), University of Oviedo, Spain; Russian Cancer Research Centre (Dr Zaridze), Moscow, Russia; Roy Castle Lung Cancer Research Programme, Cancer Research Centre (Dr Field), University of Liverpool, UK; Centre for Public Health Research (Drs Mannetje and Pearce), Massey University, Wellington, New Zealand; Occupational Cancer Research Centre (Drs McLaughlin and Demers), Toronto, Canada; The Nofer Institute of Occupational Medicine (Dr Szeszenia-Dabrowska), Lodz, Poland; The M Sklodowska-Curie Cancer Center and Institute of Oncology (Dr Lissowska), Warsaw, Poland; National Institute of Environmental Health (Dr Rudnai), Budapest, Hungary; Regional Authority of Public Health (Dr Fabianova), Banska Bystrica, Slovakia; Institute of Public Health (Dr Dumitru), Bucharest, Romania; Institute of Hygiene and Epidemiology (Dr Bencko), 1st Faculty of Medicine, Charles University, Prague, Czech Republic; Masaryk Memorial Cancer Institute (Dr Foretova), Brno, Czech Republic; Faculty of Medicine (Dr Janout), Palacky University, Olomouc, Czech Republic; The Tisch Cancer Institute and Institute for Translational Epidemiology (Dr Boffetta), Icahn School of Medicine at Mount Sinai, New York, NY; Department of Epidemiology (Dr Forastiere), ASL RomaE, Rome, Italy; The National Institute for Public Health and Environmental Protection (RIVM) (Dr Bueno-de-Mesquita), Bilthoven, the Netherlands; Institute for Risk Assessment Sciences (Drs Peters, Vermeulen, and Kromhout), Utrecht, the Netherlands; Occupational Respiratory Epidemiology (Dr Peters), School of Population Health, University of Western Australia, Perth, Australia.
Address correspondence to: Carolina Bigert, MD, PhD, Institute of Environmental Medicine, Karolinska Institutet, Solnavagen 4 10th Floor, SE-113 65, Stockholm, Sweden (carolina.bigert@ki.se).
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Abstract

Objectives: To investigate the risk of lung cancer among cooks, while controlling for smoking habits.
Methods: We used data from the SYNERGY project including pooled information on lifetime work histories and smoking habits from 16 case-control studies conducted in Europe, Canada, New Zealand, and China.

Results: Before adjustment for smoking, we observed an increased risk of lung cancer in male cooks, but not in female cooks. After adjusting, there was no increased risk and no significant exposure-response relationship. Nevertheless, subgroup analyses highlighted some possible excess risks of squamous cell carcinoma and small cell carcinoma in female cooks.
Conclusions: There is evidence that lung cancer risks among cooks may be confounded by smoking. After adjustment, cooks did not experience an increased risk of lung cancer overall. The subgroup analyses showing some excess risks among female cooks require cautious interpretation.

Cooks are exposed to a wide variety of compounds generated during cooking and frying, such as aerosols of cooking oil, combustion products, organic gaseous pollutants, and steam from the water content of the food. Emissions from high-temperature frying are classified as probably carcinogenic to humans (group 2A) by the International Agency for Research on Cancer, on the basis of limited evidence for lung cancer in humans and sufficient evidence in experimental animals.1Of particular concern in relation to carcinogenicity are polycyclic aromatic hydrocarbons (PAHs), aldehydes (eg, formaldehyde and acetaldehyde), heterocyclic amines, and other volatile compounds such as acrylamide and acrolein.1-3 Cooking and frying also increase the concentrations of fine and ultrafine particles in the air.1 The chemical composition of cooking emissions and exposure levels varies depending on the cooking oils used, the temperature, the kind of food cooked, and the method and style of cooking.1 Frying on a gas stove may cause increased occupational exposure to some of the hazardous components in cooking fumes, compared with frying on an electric stove.4,5
Several case-control studies of Chinese populations have demonstrated an exposure-response relationship between high-temperature frying and risk of lung cancer.6-9 There are also studies from other countries that indicate an increased risk of lung cancer among cooks,10-15 whereas some studies do not.16,17Many of these studies lack adequate information on individual smoking habits,14-17 and it is unknown whether the excess risk seen in many of the studies was caused by occupational exposure to cooking fumes, other occupational exposures, or by confounding from cigarette smoking. Only one study reported the prevalence of smoking among cooks, with a slightly larger proportion of regular cigarette smokers among male cooks than in the control population.12
The aim of this study was to investigate whether working as a cook is associated with an increased risk of lung cancer, while controlling for smoking using individual data on lifetime smoking habits, as well as for exposure to other occupational lung carcinogens.

METHODS

SYNERGY is a large pooled analysis of case-control studies on the joint effects of occupational carcinogens and smoking in the development of lung cancer. Detailed information about the SYNERGY project and included studies has been presented elsewhere,18 see alsowww.synergy.iarc.fr. We used the SYNERGY database including information on lifetime work histories and lifetime tobacco smoking habits from 16 case-control studies conducted in Europe (12 studies), Canada (two studies), New Zealand (one study), and China (one study). A general description of the studies included in the SYNERGY project is presented in Table 1. The data were collected in 16 countries between 1985 and 2010. The studies included are well-designed population or hospital-based case-control studies, and in one case a case-control study nested within a population cohort. In most studies, controls were frequency-matched to the cases regarding sex and age. The majority of interviews (87%) were conducted face-to-face with the subjects. The overall response rate was 82% among cases and 67% among controls. The study comprised 19,370 cases and 23,674 controls. Subjects providing incomplete information for calculating duration of jobs or cumulative smoking were omitted (472 cases and 521 controls), as well as subjects who never held a job during at least 1 year (175 cases and 200 controls), leaving 18,723 cases of lung cancer and 22,953 controls for analysis. Characteristics of the study subjects are presented in Table 2. Smoking was not more common among the cooks than among noncooks; among the controls, 63% of the cooks were current or former smokers compared with 68% among noncooks. Nevertheless, the number of pack-years in ever smokers was slightly higher among cooks; 29 years among cooks compared with 26 years in noncooks. Having ever been employed in an occupation with established lung cancer risk was slightly less common among cooks than among noncooks; among the controls, 5% of the cooks compared with 8% among noncooks ($P = 0.060$).

Identification of Cooks by Job Titles

The occupational data were originally coded according to national classifications for most studies and were recoded to the International Standard Classification of Occupations (ISCO-68).35 Cooks were identified from the ISCO-68 code ("5-31"). There were 1142 persons (670 men and 472 women) who had ever worked as a cook, among them 554 cases of lung cancer and 588 controls.

Statistical Analyses

Odds ratios (ORs) for lung cancer associated with work as a cook, and 95% confidence intervals (CIs) were estimated by unconditional logistic regression. The analyses were done separately for men and women. For all associations, three levels of adjustments were made; the first (OR1) adjusting for age group (younger than 45, 45 to 49, 50 to 54, 55 to 59, 60 to 64, 65 to 69, 70 to 74, and elder than 75 years) and study center; the second (OR2) additionally adjusting for cumulative tobacco smoking (log(cigarette pack-years + 1)) and time-since-quitting smoking cigarettes (current smokers, stopped smoking since 2 to 7 years, 8 to 15 years, 16 to 25 years, more than 26 years before interview/diagnosis, and never smokers). The pack-year variable was log-transformed because it better fitted the data. A third level of adjustment included adjusting for ever employment in an occupation with established lung cancer risk ("List A" job, yes/no). This list of occupations and industries was identified by Ahrens and Merletti in 1998 and updated by Mirabelli et al in 2001.36,37 Adjustment for "List A" job in the analyses did not influence the ORs; therefore, only OR1 and OR2 are displayed in the result tables.

Persons smoking one or more cigarettes per day for 1 or more years were coded as current smokers, including those who had stopped smoking within 2 years before diagnose/interview. Cigarette pack-years were calculated as: [SIGMA] duration x average intensity per day/20.

We repeated the analyses on lung cancer risk among cooks with restriction to never smokers, former smokers, and current smokers to explore potential residual confounding by smoking. We also analyzed the lung cancer risk among cooks by duration of work to investigate whether those with a longer duration of employment had a higher risk. The cutoffs for categories of work duration were based on the quartiles of the distribution of exposure duration among exposed controls (less than 4 years, 4 to 8 years, 9 to 22 years, more than 22 years). In addition, we stratified the analyses by the major histological subtypes of lung cancer (adenocarcinoma, squamous cell carcinoma, small cell carcinoma, and large cell carcinoma) and missing/mixed/unspecified cell type. Subjects who had never worked as a cook were the reference category in all analyses. Interaction with sex was assessed using the likelihood ratio test. *P* values for trend were obtained by including a continuous variable for duration (years) in the logistic regression model. The trend was calculated including both exposed and unexposed subjects.

Meta-analysis was used to explore extent of heterogeneity between the studies and study-specific ORs (both men and women, calculated with logistic regression, adjusted for age, sex, cigarette pack-years, and time since quitting smoking). Studies with less than five exposed cases and five exposed controls were omitted from the meta-analysis, that is INCO-Hungary, INCO-Romania, MORGEN, PARIS, and ROME. The heterogeneity was assessed using a chi-squared test with the inverse of the variance as weights. The extent of inconsistency between OR estimates was assessed as a percentage (I^2).

All analyses were conducted using Stata v. 11.0 for Windows (StataCorp LP, College Station, TX), and the command "metan" was used for the meta-analyses.

RESULTS

Overall, we observed a statistically significantly increased risk of lung cancer in male cooks (OR1 = 1.27; 95% CI, 1.09 to 1.49) but not in female cooks (OR1 = 1.16; 95% CI, 0.96 to 1.40), before adjustment for smoking. After adjusting for smoking, there was no statistically significantly increased risk of lung cancer in cooks overall, neither for men nor for women (Table 3). The OR2 for lung cancer among male cooks was 0.98 (95% CI, 0.83 to 1.17) and among female cooks 1.06 (95% CI, 0.85 to 1.31). Testing interaction with sex showed $P = 0.58$ for OR1 and $P = 0.91$ for OR2. There was no evidence of a trend in lung cancer risk with increasing duration of work as a cook ($P = 0.56$ for men [OR2] and $P = 0.86$ for women [OR2]) (Table 3).

When we analyzed the results by cell types (Table 4), there were different patterns between men and women. Among men, none of the cell types was associated with work as a cook. Among women, two of the cell types, adenocarcinoma and large cell carcinoma, showed null or even inverse associations, whereas squamous cell (OR2 = 1.73; 95% CI, 1.22 to 2.45) and small cell carcinoma (OR2 = 1.48; 95% CI, 0.98 to 2.24) showed some evidence of associations, with the highest point estimates among long-term female cooks (Table 5).

Analyses restricted to current smokers showed a borderline significantly increased risk among female cooks (OR2 = 1.49; 95% CI, 1.03 to 2.17) but no increased risk among male cooks (OR2 = 0.93; 95% CI, 0.74 to 1.17) (Table 6). For female cooks who were current smokers we also observed a statistically significant trend in lung cancer risk with duration of employment, *P* for trend 0.011 (Table 7). Analyses restricted to never smokers showed no increased risk among cooks of either sex, although the numbers of male nonsmoking cooks were so small that the OR was not very informative (Table 6).

The study-specific ORs for cooks (men and women) are shown in Fig. 1. The AUT-Munich study (Germany) was the only single study with a statistically significantly elevated OR. We observed no significant heterogeneity in lung cancer risk among cooks across the studies ($I^2 = 0.0\%$; $P = 0.94$).

DISCUSSION

We found no statistically significantly increased risk of lung cancer in cooks overall when accounting for smoking, neither for men nor for women, and there was no positive association between exposure duration and risk. Nevertheless, when analyzing separately by cell types, we found some different patterns by sex and cell type. Namely, while no cell type exhibited an increased risk for male cooks, there were some indications of increased risks of squamous cell carcinoma, and small cell carcinoma, and a low risk of large cell carcinoma in female cooks. There was no excess risk when restricting the analyses to never smokers, or to former smokers, for either sex, or among male current smokers, but there was some indication of excess risk among female current smokers.

Several factors should be taken into account in the interpretation of the current findings. An advantage of the study is that it is large and covers occupational information and detailed smoking information for the whole lifetime, for almost 19,000 cases and 23,000 controls. It included 554 exposed cases, both men and women. Many of the previously performed case-control studies on lung cancer risk among cooks comprise few exposed cases and therefore give risk estimates with wide CIs, whereas the precision in this study is higher. Cooks were identified by occupational codes. Some of them may work with cold food preparation only (with less exposure to potential carcinogens from cooking and frying), but this is likely a small fraction. In a Swedish study among cooks and other restaurant workers, the fraction who worked with cold buffets was only around 10% of the total number of cooks and cold buffet managers.38

In this study, employment in jobs known to entail increased lung cancer risk among the controls was only slightly less common among cooks compared with those who were never employed as a cook. Consequently, inclusion of this variable in the regression model did not change the risk estimates. The AUT-Munich study (Germany) was the only single study with a significantly elevated OR2 for ever working as a cook but had a low response rate among control subjects (41%), which may have resulted in selection bias if cooks were more likely than other control subjects to be nonrespondents.

Several previous studies found an excess risk of lung cancer among cooks.10-15 Among them, three case-control studies from British Columbia,10 Bombay,11and California 12 and one study based on hospital and cancer registration records and questionnaires in the United Kingdom 13 were able to control for smoking habits. The study in British Columbia did not show an increased lung cancer risk in cooks while including all histological subtypes, but only for large cell lung cancer where the precision was low with only eight exposed (chef or cook) cases. The study in Bombay also faced low statistical power with only nine exposed (cook/helper in kitchen) cases. In the Californian study, the power was better with 23 exposed (cooks) cases. The study in the United Kingdom showed an increased risk of bronchial carcinoma in cooks (RR = 2.5; 95% CI, 1.2 to 5.1). Two studies that were not able to adjust for smoking were reported by Coggon et al 14 and Pukkala et al 15; these showed an increased mortality rate from lung cancer in a cohort of male cooks who had retired from the Army Catering Corps in the United Kingdom, and an increased risk of lung cancer among male and female cooks and stewards in the Nordic countries (based on information from censuses and registration of incident cases in Denmark, Finland, Iceland, Norway, and Sweden). The study by Pukkala et al 15 also analyzed the risk for histological subtypes of lung cancer, which showed an increased standardized incidence ratio for adenocarcinoma and squamous cell carcinoma in male cooks and stewards and an increased risk of adenocarcinoma and small cell carcinoma, but not squamous cell carcinoma, in female cooks and stewards. Two earlier studies found no excess risk of lung cancer among cooks, one cohort study from Norway,16 and one study based on census and register information in England and Wales,17 although these studies lacked information on individual smoking habits. All, except the study by Pukkala et al,15 have in common that they only included men. None of the studies included exposure measurements.

In this study, we showed an increased risk of the histological subtype squamous cell carcinoma of the lung among female cooks and an almost significantly increased risk of small cell carcinoma. The reason why the effect was seen only in women and not in men is unclear. Among female cooks we also observed a statistically significant trend in risk of squamous cell carcinoma with longer duration of employment. This excess was based on a secondary subgroup analysis and must be interpreted with caution. The two previous studies of histological subtypes of lung cancer among cooks do not support our results. One showed no excess risk of squamous cell carcinoma among cooks (only men were included),10 and the other showed an excess risk of squamous cell carcinoma in male but not in female cooks.15

Cooking fumes are suspected to cause an increased risk of lung cancer in Chinese women involved in household cooking, where exposure-response relationships were shown between frequency and duration of high-temperature frying and increased risk of lung cancer.6-9 Thus, an important body of evidence, a large part of which comes from studies conducted in China, seems to support an increased lung cancer risk due to exposure from cooking activities. There are major differences in cooking practices between Asian and Western countries, including type of food cooked, the method of cooking, type of cooking oil used, ventilation in the kitchen, and the type of fuel used. Burning of biomass or coke in poor ventilated kitchens causes a high exposure to carcinogenic PAHs.1 In this pooled study, the only study included from China (Hong Kong) did not show an increased lung cancer risk among cooks (Fig. 1).

Polycyclic aromatic hydrocarbons and higher aldehydes have been detected in the breathing zone of cooks during frying.5,39 Personal measurements of the levels of PAHs and higher aldehydes were performed in three restaurants in Norway during the four peak hours regarding the number of customers.39Naphthalene was the dominant PAH in cooking fumes and was detected within the range of 0.05 to 0.27

[mu]g/m 3 air, whereas the levels of mutagenic aldehydes were between 1.03 and 17.7 [mu]g/m^3 air.

Smoking is a risk factor for all histological types of lung cancer. The epidemiological evidence relating smoking to lung cancer histological types demonstrates that the association is strongest for small and squamous cell carcinoma, intermediate for large cell carcinoma, and weaker but still very strong for adenocarcinoma, and this holds in both sexes.40 The excess risk of lung cancer overall among female cooks when analyses were restricted to current smokers, as well as an exposure-response relationship with work duration, and the fact that smoking is associated particularly with the two histological subtypes of lung cancer for which we noted an increased risk (squamous cell carcinoma) and possibly increased risk (small cell carcinoma) among women, indicates the possibility of a joint effect with smoking, as well as of residual confounding from smoking or confounding because of environmental tobacco smoke. There is also a possibility that women may be more sensitive than men to carcinogens in cooking fumes or that the exposure situation in the kitchen may differ between men and women, although this is quite speculative. It could also be a chance finding as a result of multiple testing. Nevertheless, emissions formed while cooking and frying at high temperatures are known to contain carcinogens such as PAHs and mutagenic aldehydes. It seems important to continue the efforts to reduce the exposure to these emissions as much as possible, for instance by the use of adequate local exhaust ventilation. Nevertheless, the most important measure for preventing lung cancer in cooks would probably be reduction of smoking.

CONCLUSIONS

We did not detect an increased risk of lung cancer overall among male or female cooks, when lifetime history of tobacco smoking was taken into account. Subgroup analyses highlighted some possible excess risks of squamous cell carcinoma and small cell carcinoma in female cooks. There is evidence that lung cancer risks among cooks may be confounded by smoking.

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