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Factors mediating the association between socioeconomic status and lung cancer risk

Thomas MATUKALA NKOSI[a,b,c]*, Marie-Elise PARENT[a,b], Jack SIEMIATYCKI[d], Belinda NICOLAU[a], Marie-Claude ROUSSEAU[a,b]

[a]*Institut National de la Recherche Scientifique (INRS)-Institut Armand-Frappier, Laval, Québec, Canada*
[b]*Université de Montréal, Montréal, Québec, Canada*
[c]*Université Laurentienne, Sudbury, Ontario, Canada, Institut Supérieur des Techniques Médicales de Kinshasa, Kinshasa, République Démocratique du Congo, Institut Supérieur des Techniques Appliquées de Kasangulu, Kasangulu, Kongo Central, République Démocratique du Congo*
[d]*Research Center of the Hospital Center of the University of Montreal, Montréal, Québec, Canada*

RESUME:
Le revenu, l'éducation et l'emploi sont souvent utilisés comme indicateurs du statut socio-économique(SSE), chacun renseignant probablement sur des dimensions différentes. Ce n'est cependant pas clair si l'association entre chaque indicateur du SSE et le cancer du poumon est médiée par les mêmes facteurs et avec la même ampleur. Cette étude évalue comment les facteurs comme le tabagisme, l'alimentation et les expositions professionnelles peuvent expliquer l'association entre le SSE et le risque de cancer du poumon.

Mots clés : Statut socio-économique, éducation, revenu, emploi, cancer du poumon, facteurs de risque intermédiaires

ABSTRACT :
Income, education and occupation are commonly used SES indicators, each probably capturing different dimension. It is unclear whether the association between each SES indicator and lung cancer is mediated by the same factors and to the same extent. This study evaluates how factors such as smoking, diet, and occupational exposures mediate the association between SES and lung cancer risk

Keywords : socioeconomic status, income, education, occupation, diet, lung cancer, mediators

***Adresse des Auteur(s)**
THOMAS MATUKALA NKOSI, *Institut National de la Recherche Scientifique (INRS)-Institut Armand-Frappier, Laval, Québec, Canada, Université de Montréal, Montréal, Québec, Canada, Université Laurentienne, Sudbury, Ontario, Canada, Institut Supérieur des Techniques Médicales de Kinshasa, Kinshasa, République Démocratique du Congo, Institut Supérieur des Techniques Appliquées de Kasangulu, Kasangulu, Kongo Central, République Démocratique du Congo,*
Marie-Elise PARENT, *Institut National de la Recherche Scientifique (INRS)-Institut Armand-Frappier, Laval, Québec, Canada, Université de Montréal, Montréal, Québec, Canada,*
Jack SIEMIATYCKI, *Research Center of the Hospital Center of the University of Montreal, Montréal, Québec, Canada,*
Belinda NICOLAU, *Institut National de la Recherche Scientifique (INRS)-Institut Armand-Frappier, Laval, Québec, Canada,*
Marie-Claude ROUSSEAU, *Institut National de la Recherche Scientifique (INRS)-Institut Armand-Frappier, Laval, Québec, Canada, Université de Montréal, Montréal, Québec, Canada,*

I. INTRODUCTION

Lung cancer is the most frequent malignancy and the main cause of cancer death worldwide.[1,2] Individuals with a lower socioeconomic status (SES) have often been reported to have a higher risk of developing lung cancer,[3-6] and smoking seems to be the main factor through which this association occurs.[1,3,6] It has been suggested that the inverse association between SES and lung cancer risk[1,4,7-10] could be the result of a suboptimal adjustment for smoking behaviour.[1,4,9] Indeed, in a previous study, we observed that the relation between income – frequently used as an indicator of SES – and lung cancer gradually disappeared when moving from a simple to a more detail adjustment for cigarette smoking behaviour.[11]

Moreover, other factors associated with lung cancer risk, such as occupational exposures and diet, could play a mediating role in the association between SES and lung cancer.[1,4,12] Some occupational exposures have been identified as definite or probable carcinogens, with lung being one of the target organs.[13] As for diet, an extensive review of the epidemiological evidence concluded that a decreased lung cancer risk was probably associated with a diet rich in fruit; there was limited suggestive evidence for a protective effect from non-starchy vegetables.[14] Occupational exposures and diet are very likely related to SES, making it possible for these factors to mediate the association between SES and lung cancer risk.

In addition, income, education and occupation are commonly used as indicators of SES,[15] and each of these may capture different dimensions of SES. It is unclear whether the association between each SES indicator and lung cancer would be mediated by the same factors and to the same extent. Furthermore, any mediating effect could vary according to gender.[15]

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Using data from a Montreal-based case-control study, we evaluated how factors such as smoking, diet, and occupational exposures mediate the association between SES and lung cancer risk. The potential mediating effects were assessed for three different markers of SES (i.e., income, education, and occupational class) and for both men and women.

II. MATERIAL ET METHODS

II.1. Study design and population

Data from a population-based case-control study of environmental risk factors for lung cancer were used. The study population included 1,203 cases and 1,513 controls, all Canadian citizens aged between 29 and 75 years and residing in Greater Montreal. Incident cases of primary lung cancer were identified from pathology departments lists across the 18 hospitals in the Montreal metropolitan area between January 1996 and December 1997. Population controls were randomly selected from the electoral lists. In Quebec (Canada), the electoral lists were maintained through periodic household enumerations until 1994. Since then, they have been continually updated and include almost all Canadian citizens aged 18 and over residing in the province.[16,17] Controls were frequency-matched to cases based on their age distribution (5-year categories), sex, and electoral district (each including about 40,000 voters). Response rates were 84% and 71% for cases and controls respectively. Proxy respondents, generally the spouse, provided information for 38% of cases and 8% of controls. Ethical approval was obtained from all the participating hospitals and institutions prior to collecting data.

Face-to-face interviews were conducted by trained interviewers. Information was elicited on a wide range of factors, including socio-demographic characteristics, smoking, diet, and a detailed occupational history.

II.2. Education

The highest level of education attained was classified in 3 categories: primary, secondary and post-secondary educational level. Information on education was available for 2,646 subjects.

II.3. Census income

The median household income was extracted from the 1996 Census data using the postal code at the time of diagnosis for cases and at the time of interview for controls. The continuous variable was categorized as follows: <$30,000; $30,000 - $49,999; and ≥ $50,000. Census income information was available for all 2,716 subjects.

II.4. Occupational class

Detailed information on each job held for at least 6 months was collected. An industrial hygienist had initially reviewed each job and assigned an occupational code based on the International Standard Classification of Occupations 1968 (ISCO-68).[18] For the purpose of the current analysis, this code was translated into the 1988 classification (ISCO-88), the first digit of which enables a ranking of occupations into 10 major groups.[18] These can be further classified into four skill levels corresponding to the following major groups: 1) elementary occupations; 2) clerks, service workers and shop and market sales workers, skilled agricultural and fishery workers, craft and related workers, plant and machine operators and assemblers; 3) technicians and associate professionals, and; 4) professionals. Occupational class was first defined by the ISCO-88 major group held for the longest time throughout each participant's employment history. Then, those were combined into categories adapted from the ISCO-88 skill levels. These three categories were: professionals, service or job related workers, and elementary workers. A fourth category of housewives or homemakers was also added and treated separately for women. The category "Professionals" included legislators, senior officials and managers. Service and related workers were comprised of clerks, service workers and shop and market sales workers, skill agricultural and fishery workers, craft and related workers and plant, and machine operators and assemblers. For those whose pension and/or illness accounted for the longest duration, the longest cumulative skill level in active employment was selected. Occupational class was available for 2,603 subjects.

II.5. Potential mediators

II.5.1. Smoking

A detailed lifetime smoking history was elicited, capturing information on smoking periods, amounts, durations, and interruptions. As suggested by Leffondré et al. as the model providing the best fit in this database,[19] we used three variables for smoking adjustment: a binary variable indicating whether the subject has ever smoked or not, a continuous variable indicating the lifetime number of cigarette–years (natural log transformed), and a categorical variable for the time since smoking cessation (0-2 years, 3-5 years, 6-10 years, ≥ 10 years). A smoker was defined as someone who had smoked at least 100 cigarettes in their lifetime; an ex-smoker as someone who had stopped smoking at least 2 years before the interview.

II.5.2. Occupational exposures

The occupational exposure assessment approach has been described in details elsewhere.[17] In brief, based on the detail description of each job, a team of chemists / industrial hygienists assigned potential exposure to 294 chemicals. Chemists had to assign, for each substance, their level of certainty that the exposure had actually occurred (possible, probable, definite), the number of hours per day and the relative concentration of exposure into three levels (low, medium, high). To define the level of concentration of exposure, hygienists estimated that the average concentration was about 3 times higher than that of low concentration and a high concentration was about 9 times greater than a low concentration. Non-exposure corresponded to the normal level found in the general environment.

For purposes of analysis, a composite exposure index was created to summarize, for each participant, the cumulative exposure to each substance on a continuous scale. The composite exposure index was calculated considering only definite and probable exposures that took place at least five years prior to recruitment. It was obtained by adding across all jobs held, and for each substance, the following product: [concentration level of the substance X proportion of time exposed in employment X number of years of exposure in

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employment]. The concentration levels low, medium and high were assigned values of 1, 3 and 9, respectively.

The exposure index specific to each substance was then categorized into three levels: no exposure, low exposure, and high exposure. The unexposed group included subjects who had not been exposed to the identified substance in any of the jobs they had occupied. Exposed subjects were divided into tertiles according to the distribution of exposures among controls. Individuals allocated in the lower two tertiles of the distribution were assigned a low exposure level, while the others were considered to have a high exposure level.

II.5.3. Diet

As described in detail elsewhere[20], study participants were administered a food frequency questionnaire that mainly focused on carotenoid-rich foods consumed 2 years earlier. It covered 77 food items, including 49 fruit and vegetables which were grouped into 25 individual statements. Frequency of intake, in terms of a typical portion size, was reported as “7 or more times per week”, “4 to 6 times per week”, “1 to 3 times per week”, “1 to 3 times per month” and “never or less than once per month”. The mid-point of each frequency category was used to assign a weekly frequency of intake on each food. A continuous variable, representing the weekly intake of fruit and vegetables rich in antioxidants, was used in the present analyses.

II.6. Statistical analysis

To enable comparisons, we conducted statistical analyses on the 2,533 study participants for whom information on all three indicators of socioeconomic status (education, census income, occupational class) were available. We first described participants according to their socio-demographic and economic characteristics, smoking behavior, diet, and occupational exposures. Frequency distributions and means (and standard deviations) were calculated according to case/control status.

In order to evaluate which set of variables explained best the association between each of the SES indicators and lung cancer risk, we conducted logistic regression analyses for the estimation of odds ratios (OR) and 95% confidence intervals (CI).

Several models were built. Model 1 included a set of socio-demographic characteristics, i.e., age (in 4 categories), sex, respondent type (self / proxy), and country of origin (Canada / other). Model 2 included all variables from Model 1 plus three smoking parameters: ever / never smoking, natural log of cigarette-years, and time since smoking cessation. Model 3 included all variables from Model 2 plus diet, i.e., the weekly frequency of use of carotenoid-rich fruit and vegetables. Model 4 included all variables from Model 2 plus selected occupational exposures (described below). Model 5 included all variables from Model 2 as well as diet and the same occupational exposures as those described for Model 4.

To model the occupational exposures, we first selected 5 occupational chemicals of particular relevance to the present analysis (asbestos, soot, crystalline silica, benzo (a) pyrene, diesel engine emissions). These were declared to be either probable or definite carcinogens by IARC, their prevalence was at least 5% percent among controls, and they were associated with lung cancer in our study. We then verified that each of the 5 selected occupational exposures could change the odds ratios between each of the SES indicators and lung cancer by at least 10%. As a result, models 4 and 5 assessing the association for educational level and lung cancer among men were adjusted for diesel engine emissions, while model 4 et 5 focusing on the occupational class were adjusted for crystalline silica. For women, and for all three SES indicators, models 4 and 5 were adjusted for crystalline silica. Exposures indices modeled as “ever/never” led to a better fit than the use of 3 categories (unexposed, low, high exposure), based on Akaike’s Information Criterion (AIC). Therefore, binary exposure variables were used for all occupational exposures.

In the regression analyses, the lowest levels of education (primary) and census income (< $30,000) were used as reference categories. However, "professionals" were used as the reference category for occupational social class, because there were insufficient numbers in the category of elementary workers.

We calculated the p-value for linear trends across the SES indicator categories and lung cancer risk. This was performed by including an ordinal variable as a continuous covariate in the regression models. The “homemakers” category was excluded from the p-value estimations for occupational social class among women.

Finally, the goodness-of-fit of the various models was assessed using the Akaike's Information Criterion (AIC), computed as [-2 log likelihood + 2*(number of parameters estimated in the model)]. Comparisons of AIC across models allowed to identify which set of variables was a better predictor of lung cancer risk. Overall, smaller values of the AIC for a given dataset indicate better fit, but an absolute difference less than 4 is considered as minor, and an absolute difference more than 10 is seen as important. Any difference under 0 indicates better fit while any difference above 0 indicates worse fit.[21]

All statistical analyses were performed using the Statistical Program for the Social Sciences (SPSS) program (version 16.0).

III. RESULTS

Study participants were predominantly men, over 50 years of age, and originating from Canada (Table 1). More controls, men and women, than cases responded themselves to the interview questions. Cases were more likely to be smokers, had smoked more cigarettes on average, and consumed less carotenoid-rich fruit and vegetables weekly than controls. Overall, more cases than controls had been exposed to the 5 occupational substances retained for study, and the lifetime prevalence of occupational exposures were higher among men than women. Diesel exhaust and crystalline silica were the most common occupational exposures among men and women, respectively. As for the indicators of SES, cases had

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lower levels of education and income irrespective of gender. Among men and women, there were lower proportions of professionals among cases than controls. "Homemakers", an occupational class added among women because there were several study subjects in this situation, was nearly twice as common among cases than controls.

Results from the logistic regression analyses (Tables 2 and 3) suggested a strong, significant association between SES and lung cancer risk, regardless of gender or SES indicator, when the basic model (Model 1) was applied. Subjects with the lowest educational level, income and occupational class had the highest risk of lung cancer. Moreover, there was evidence of a dose-response relationship with each of the three SES indicators and lung cancer risk.

Adding the smoking parameters (Model 2) considerably attenuated the associations for each of the SES indicators among both men and women. AIC values were consistent with an important improvement in the fit of the models when the different smoking dimensions were considered. After adjusting for smoking, none of the SES-lung cancer associations among men achieved statistical significance, except for those classified in the services and related workers category. A two-fold excess risk remained among women classified as homemakers.

When diet, as represented by carotenoid-rich foods, was further added as a covariate (Model 3), odds ratios generally tended to move further toward the null. This suggests that diet contributed independently as a mediator in the SES-lung cancer association, in addition to smoking. AIC values were reduced by a magnitude of about 10 units among men, depending on the SES indicator, consistent with a relatively important effect of diet. However, the improvement in the fit of the models based on women was particularly important when diet was introduced, with reductions of the AIC in the order of 40 units. Model 3 provided the best fit between census income and lung cancer among men, and between all three SES indicators and lung cancer among women.

Replacing the diet variable by relevant occupational exposures (Model 4) generated results that varied according to the SES indicator. Indeed, among men, adding occupational variables moderately improved the fit for the associations of education and occupational class with lung cancer. However, this had no effect on the model fit for the association between census income and lung cancer since there were no selected occupational exposures for this indicator, based on the ≥ 10% variation in the OR criterion. Overall, Model 4 provided the best fit for the association between education and lung cancer. Among women, adding crystalline silica to the models resulted in a slight worsening of the fit for all SES indicators.

Model 5 included the basic variables, along with smoking, diet and occupational exposures. This "full model" turned out to provide the best fit to the data for the relation between occupational class and lung cancer risk among men.

Table 1: Distribution of cases and controls according to selected characteristics (N = 2533)

Characteristics	Men Cases N = 694	Men Controls N = 886	Women Cases N = 413	Women Controls N = 540
Age in years (%)				
29-49	40 (5.8)	43 (4.9)	52 (12.6)	73 (13.5)
50-59	148 (21.3)	158 (17.8)	126 (30.5)	148 (27.4)
60-69	332 (47.8)	449 (50.7)	147 (35.6)	204 (37.8)
≥ 70	174 (25.1)	236 (26.6)	88 (21.3)	115 (21.3)
Country of origin (%)				
Canada	575 (82.9)	630 (71.1)	378 (91.5)	421 (78.0)
Other	119 (17.1)	256 (28.9)	35 (8.5)	119 (22.0)
Education (%)				
Primary	312 (45.0)	315 (35.6)	143 (34.6)	132 (24.4)
Secondary	289 (41.6)	366 (41.3)	218 (52.8)	241 (44.6)
Post-secondary	93 (13.4)	205 (23.1)	52 (12.6)	167 (30.9)
Census income (%)				
< 30,000	351 (50.6)	397 (44.8)	205 (49.6)	172 (31.9)
30,000-49,999	261 (37.6)	345 (38.9)	158 (38.3)	248 (45.9)
≥ 50,000	82 (11.8)	144 (16.3)	50 (12.1)	120 (22.2)
Occupational social class (%)				
Professionals	163 (23.5)	294 (33.2)	50 (12.1)	148 (27.4)
Services and related workers	452 (65.1)	498 (56.2)	179 (41.2)	234 (43.3)
Elementary occupations' workers	79 (11.4)	94 (10.6)	24 (5.8)	24 (4.4)
Homemakers	-	-	169 (40.9)	134 (24.8)
Respondent type (%)				
Self	437 (63.0)	801 (90.4)	283 (68.5)	521 (96.5)
Other	257 (37.0)	85 (9.6)	130 (31.5)	19 (3.5)
Smoking status (%)				
Never	17 (2.4)	154 (17.4)	29 (7.0)	269 (49.8)
Former smoker	410 (59.1)	503 (56.8)	226 (54.7)	176 (32.6)
Current smoker	267 (38.5)	229 (25.8)	158 (38.3)	95 (17.6)
Cigarette-years (mean ± SD)*	1521.39 ± 880.3	828.8 ± 794.0	995.31 ± 591.1	315.4 ± 473.9
Years since cessation of smoking (mean ± SD)**	0.77 ± 1.23	1.49 ± 1.43	0.46 ± 0.98	0.71 ± 1.21
Weekly servings of fruit and vegetables (mean ± SD)	28.9 ± 18..6	38.3 ± 20.2	26.7 ± 15.2	39.5 ± 15.2
Lifetime prevalence of occupational	194	200 (22.6)	1 (0.2)	6 (1.1)

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exposure (%)	(28.0)	67 (7.6)	1 (0.2)	1 (0.2)
Asbestos	81	216 (24.4)	40 (9.7)	40 (7.4)
Soot	(11.7)	394 (44.5)	15 (3.6)	21 (3.9)
Crystalline	204	223 (25.2)	5 (1.2)	10 (1.9)
Silica	(29.4)			
Diesel	361			
emissions	(52.0)			
	214			
Benzo(a)pyrene	(30.8)			

**Among ever smokers*
***Among former smokers*

Table 2: Odds ratios (OR) and 95% confidence intervals (CI) for the associations between each of the three SES indicators and lung cancer risk (Men)

	Cancer status: Controls (N)	Cancer status: Cases (N)	Model 1 OR (95% CI)	Model 2 OR (95% CI)	Model 3 OR (95% CI)	Model 4 OR (95% CI)	Model 5 OR (95% CI)	Best model based on AIC
Variables in each model			age, sex, respondent type and country of origin	variables in model 1 + smoking*	variables in model 2 + diet**	variables in model 2 + selected occupational exposures***	variables in model 2 + diet + selected occupational exposures***	
Educational level								
Primary	312	315	Reference	Reference	Reference	Reference	Reference	Model 4
Secondary	289	366	0.70 (0.55 – 0.89)	0.80 (0.61 – 1.04)	0.84 (0.64 – 1.09)	0.83 (0.64 – 1.09)	0.87 (0.66 – 1.14)	
Post-secondary	93	205	0.45 (0.33 – 0.62)	0.77 (0.54 – 1.10)	0.83 (0.58 – 1.18)	0.84 (0.59 – 1.21)	0.91 (0.63 – 1.31)	
P for trend			**< 0.001**	**0.087**	**0.209**	**0.246**	**0.474**	
AIC			**1945**	**1675**	**1665**	**1659**	**1664**	
Census income								
< 30,000	351	397	Reference	Reference	Reference	Reference-	Reference	Model 3
30,000-49,999	261	345	0.94 (0.74 – 1.18)	1.16 (0.90 – 1.51)	1.19 (0.92 – 1.54)	1.16 (0.90 – 1.51)	1.19 (0.92 – 1.54)	
≥ 50,000	82	144	0.67 (0.48 – 0.93)	0.84 (0.59 – 1.21)	0.88 (0.62 – 1.27)	0.84 (0.59 – 1.21)	0.88 (0.62 – 1.27)	
P for trend			**0.031**	**0.765**	**0.982**	**0.765**	**0.982**	
AIC			**1965**	**1675**	**1664**	**1675**	**1664**	
Occupational class								
Professionals	294	163	Reference	Reference	Reference	Reference	Reference	Model 5
Services and related workers	498	452	1.61 (1.26 – 2.06)	1.32 (1.00 – 1.73)	1.27 (0.96 – 1.67)	1.24 (0.94 – 1.64)	1.20 (0.90 – 1.58)	
Elementary occupations' workers	94	79	1.49 (1.01 – 2.19)	1.09 (0.72 – 1.67)	1.01 (0.66 – 1.55)	0.97 (0.63 – 1.50)	0.90 (0.58 – 1.40)	
Homemakers	-	-	-	-	-	-	-	
P for trend			**0.002**	**0.115**	**0.490**	**0.634**	**0.907**	
AIC			**1956**	**1674**	**1664**	**1669**	**1659**	

* Smoking was parameterized as follows: smoking (ever/never), natural log of cigarette-years, and time since smoking cessation.
** Diet was defined as the weekly portions of carotenoid-containing fruit and vegetables.
*** Occupational exposures selected were those changing the OR for the specific SES indicator by ≥ 10%: diesel engine emissions for educational level, no occupational exposure for census income, and crystalline silica for occupational class.

Table 3: Odds ratios (OR) and 95% confidence intervals (CI) for the associations between each of the three SES indicators and lung cancer risk (Women)

	Cancer status: Controls (N)	Cancer status: Cases (N)	Model 1 OR (95% CI)	Model 2 OR (95% CI)	Model 3 OR (95% CI)	Model 4 OR (95% CI)	Best model based on AIC
Variables in each model			age, sex, respondent type and country of origin	variables in model 1 + smoking*	variables in model 2 + diet**	variables in model 2 + crystalline silica	
Educational level							
Primary	143	132	Reference	Reference	Reference	Reference	Model 3
Secondary	218	241	0.83 (0.59 – 1.18)	1.07 (0.71 – 1.61)	1.16 (0.76 – 1.78)	1.07 (0.71 – 1.62)	
Post-secondary	52	167	0.29 (0.19 – 0.46)	0.62 (0.36 – 1.06)	0.74 (0.42 – 1.29)	0.62 (0.36 – 1.08)	
P for trend			**<0.001**	**0.112**	**0.352**	**0.108**	
AIC			**1095**	**865**	**825**	**867**	
Census income							
< 30,000	205	172	Reference	Reference	Reference	Reference	
30,000-49,999	158	248	0.60 (0.44 – 0.82)	0.80 (0.55 – 1.15)	0.80 (0.55 – 1.18)	0.79 (0.55 – 1.15)	Model 3
≥ 50,000	50	120	0.40 (0.26 – 0.62)	0.62 (0.38 – 1.02)	0.73 (0.44 – 1.21)	0.63 (0.38 – 1.03)	
P for trend			**<0.001**	**0.051**	**0.172**	**0.053**	
AIC			**1112**	**867**	**826**	**869**	
Occupationalclass							
Professionals	148	50	Reference	Reference	Reference	Reference	Model 3
Services and related workers	234	179	2.07 (1.37 – 3.13)	1.17 (0.72 – 1.90)	1.02 (0.62 – 1.68)	1.14 (0.70 – 1.86)	
Elementary occupations' workers	24	24	2.43 (1.16 – 5.10)	1.13 (0.48 – 2.67)	0.86 (0.35 – 2.11)	1.00 (0.41 – 2.46)	
Homemakers	134	169	3.80 (2.45- 5.88)	2.44 (1.45 – 4.10)	2.06 (1.21 – 3.51)	2.43 (1.45 – 4.09)	
P for trend excluding homemakers			**0.001**	**0.624**	**0.883**	**0.971**	
AIC			**1094**	**855**	**816**	**857**	

AIC: Akaike's Information Criterion
* Smoking was parameterized as follows : smoking (ever/never), natural log of cigarette-years, and time since smoking cessation.
**Diet was defined as the weekly portions of carotenoid-containing fruit and vegetables.

IV. DISCUSSION

This study explored the associations between three indicators of SES – education, income and occupational class – and the risk of the lung cancer, and whether these associations were mediated by risk factors other than smoking, such as diet and occupational exposures. We observed that the three SES indicators were significantly related to lung cancer risk when adjusting only for age, country of origin, and type of respondent. Introducing one potential mediating factor at the time, i.e., smoking, diet and occupational exposures generally tended to bring the odds ratios for association between SES indicators and lung cancer progressively toward the null. Intake of carotenoid-rich foods appeared to be an important mediating factor in addition to smoking, for all three SES indicators and among both men and women. This mediating effect appeared to be particularly strong for women. Once these two factors were taken into account, occupational exposures exerted an additional modest mediating effect, among men only, in the relations between educational level and occupational class, and lung cancer risk. The successive adjustments with the three potential mediating factors virtually eliminated the SES-lung cancer risk associations. One notable exception is that of the female homemakers, for whom a two-fold excess in risk of lung cancer persisted even when the potential mediators smoking and diet were added to the models. This suggests that factors other than those measured here would be implicated in this relationship.

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Of all the factors examined, smoking played the largest mediating role between SES and lung cancer, followed by diet, especially among women. Occupational exposures played a minor mediating role for men and did not play a role for women. Overall, the study showed that each of the three mediators has the potential of exerting an independent effect in the SES - lung cancer risk association. The mediating effects were generally similar, notwithstanding the SES indicator being examined.

Whereas another study examined whether lung cancer risk was more strongly associated with income or with occupation,[22] we used three common indicators of socioeconomic status, i.e., education, census income, and occupational class.[3,15,23] Our study corroborates the findings of most other studies in this field by showing that, regardless of gender or the SES measure chosen, smoking plays a fundamental role in the relationship between SES and the risk of lung cancer.[1,24,25] However, our analyses suggest that smoking is unlikely to be the unique mediating factor. In our study as in others[1,4,9] the possibility of residual confounding due to smoking cannot be entirely ruled out. However, our parameterization of the several dimensions of smoking, previously demonstrated to provide the best fit at least in our dataset[19] is more detailed than used in previous investigations. We thus believe that residual confounding by smoking might have played a lesser role than in studies based on cruder smoking adjustments.

Results from this study also demonstrate, as observed[26,14,27,28] or suggested[4] previously, that dietary factors play an important role in the relationship between SES and lung cancer risk. The mediating effect of dietary factors was apparent for all of our SES indicators and particularly strong among women. In a study by Kreiger et al.[29] the relations between education, occupational class, and lung cancer were also found to be associated with diet. In our study, diet held the second largest mediating role, after smoking.

While it has been proposed that studies be conducted to investigate the role of occupational exposures as potential mediators of the association between SES and lung cancer risk,[1,30] to our knowledge only three studies, including ours, have formally addressed this issue.[30,31] Our results are consistent with a moderate mediating effect of occupational exposures such as diesel engine emissions and crystalline silica in the relation between SES, as measured by education and occupational class, and lung cancer risk among men. This effect was additional to that of smoking. Pastorino et al.[31] also reported that occupational exposures were minor determinants in the relationship between incidence of lung cancer and social class (based on the last occupation), after adjustment for smoking[31]. By contrast, Van Loon et al.[30] who examined the role of occupational exposure to asbestos, paint dust, polycyclic aromatic hydrocarbons, and welding fumes observed no such mediating effect with regard to education and social class among male workers. We found no other study attempting to evaluate the potential mediating role of occupational exposures among women. Our results suggest that crystalline silica does not play a mediating role in the SES-lung cancer association among them. The low prevalence of occupational exposures of potential relevance among our female subjects might explain our findings. Overall, the evidence on the role of occupational exposures as mediating factors remains sparse.

Our study has some limitations. While we used three different SES indicators, each of them entailed measurement error which inevitably resulted in subjects' misclassification. For instance, the education categories used in our analyses did not distinguish between subjects who completed a given educational level versus those who did not. Information on income was drawn from census data. Since it is known that bias might occur when estimating individual parameters from aggregated data,[32] using census income may have classified together subjects with different characteristics. With respect to the occupational class, it is possible that some of the occupational titles coded according to the ISCO-88, which was used to derive skill levels, might have been imperfect. Our industrial hygienists coded occupational titles according to the ISCO-68 using the detail job description, but the cross-walk between ISCO-68 and ISCO-88 might have introduced some errors. Finally, the three indicators probably measured somewhat different dimensions of SES. As such, they would not be expected to yield identical results. Nevertheless, we believe that the general coherence of our findings across indicators gives credibility to our findings.

Likewise, measurement error cannot be ruled out among the potential mediators: smoking, diet and occupational exposures. The extent of misclassification may have varied according to the different variables. If this was the case, it is possible that the mediating effect of a factor, e.g., diet, may have been underestimated as compared to others. As compared to other studies, information on several dimensions of smoking behavior was available, very likely resulting in a better characterization of this factor. Occupational exposures were modeled with simple binary variables indicating ever exposure. This might not have allowed us to pick-up mediating effects due to high levels of exposure. However, the optimal modeling was verified with 3-level occupational exposure index variables, and the fit was better with binary variables based on the AIC.

While this study enabled us to assess the potential mediating effect of three different factors, it is likely that other factors not considered here could be implicated. For example, alcohol intake or genetics factors which have already been found to be associated with both SES and lung cancer risk[27,28] could have been of interest.

V. CONCLUSION

Our results suggest that the three factors studied here, i.e., smoking, intake of carotenoid-containing fruit and vegetables, and occupational exposures, have an independent mediating effect on the association between SES and the risk of lung cancer. Once all three factors were taken into account, the SES – lung cancer risk association virtually disappeared. This generally held true for the three SES indicators used, as well as among both men and women. The strongest mediating effect was from smoking, followed by diet, and, to a much lesser extent, occupational exposures. Future studies investigating the SES-lung cancer risk association should definitely take into account the different dimensions of smoking. Dietary factors also need to be taken into account in order to make correct inferences. Firm recommendations over occupational exposures will require additional evidence.

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