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Education and Lung Cancer Among Never Smokers

Gwenn Menvielle

INSERM UMR_S 1136 Pierre Louis Institute of Epidemiology and Public Health Paris, France

Thérèse Truong, Fatima Jellouli, and Isabelle Stücker

Inserm U1018 Center for Epidemiology and Population Health Villejuif, France

Hermann Brenner

Division of Clinical Epidemiology and Aging Research German Cancer Research Center (DKFZ)
Heidelberg, Germany

John K. Field

The University of Liverpool Cancer Research Centre Institute of Translational Medicine Liverpool,
United Kingdom

H. Dean Hosgood, Qing Lan, and Maria Teresa Landi

Division of Cancer Epidemiology and Genetics National Cancer Institute Rockville, MD

Rayjean J. Hung

Lunenfeld-Tanenbaum Research Institute of Mount Sinai Hospital, Toronto, Canada

Philip Lazarus

Department of Pharmaceutical Sciences Washington State University College of Pharmacy
Spokane, WA

John McLaughlin

Samuel Lunenfeld Research Institute Mount Sinai Hospital Toronto, Canada

Hal Morgenstern

Department of Epidemiology School of Public Health University of Michigan Ann Arbor, MI

Joshua E. Muscat

Department of Public Health Sciences Penn State College of Medicine Hershey, PA

Alberto Ruano-Ravina

Department of Preventive Medicine and Public Health University of Santiago de Compostela
Santiago de Compostela, Spain

Ann G. Schwartz

Karmanos Cancer Institute Wayne State University Detroit, MI

Adeline Seow

Saw Swee Hock School of Public Health National University of Singapore Singapore

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Margaret R. Spitz

Dan L. Duncan Cancer Center Houston, TX

Adonina Tardon

Departamento de Medicina University of Oviedo Campus del Cristo s/n Oviedo, Asturias, Spain

Zuo-Feng Zhang

Department of Epidemiology Fielding School of Public Health University of California Los Angeles, CA

Danièle Luce

Inserm U1085 Irset, 97110 Pointe-à-Pitre Guadeloupe, French West Indies
gwenn.menvielle@inserm.fr

To the Editor:

Socioeconomic inequalities in lung cancer incidence have been consistently reported. Contradictory findings, however, have been found regarding the extent to which smoking accounts for these inequalities.^{1,2} A recent study concluded that smoking alone accounted for all socioeconomic inequalities in lung cancer risk, and that the remaining association between socioeconomic status and lung cancer risk reported in previous studies after adjustment for smoking was due to incomplete adjustment for smoking.³ As residual confounding by smoking can never be ruled out, we investigated inequalities in lung cancer risk in the subgroup of never-smokers.

We used data from 14 case-control studies participating to the International Lung Cancer Consortium from Europe, North America, and Asia. The association of lung cancer risk with education (up to lower secondary, upper secondary, tertiary) was assessed with unconditional logistic regression using generalized estimating equations models to account for heterogeneity that may be due to variability between study populations.

In total, 484 male cases, 2644 male controls, 1209 female cases, and 3283 female controls were included. Among men, higher lung cancer risk was reported among the least educated men in all regions, except in Spain where the opposite association was observed (Table; eTables 1–3, <http://links.lww.com/EDE/A833>). The increased odds ratio was appreciable among men in the intermediate education group in France and Italy. Among women, little association between education and lung cancer risk was reported, with an odds ratio for women in the intermediate education group close to 1.00 in all models. We found larger inequalities in studies with population-based controls than with hospital-based controls.

Although we conducted analyses among never-smokers, residual confounding by smoking cannot be totally ruled out. Some never-smokers may actually be former smokers. However, studies consistently reported a high agreement between self-reported and biologically assessed smoking status, with differences limited to light smokers or ex-smokers who stopped a long time ago and no difference by socioeconomic characteristics.⁴ Smoking status may also be more accurately reported among cases, which would lead to an underestimation of the association. According to Nyberg et al,⁴ this misreporting could explain an association of 1.12 between education and lung cancer in the situation where

there is no association, and we found more pronounced associations among men who had never smoked. All this evidence suggests that this misclassification is limited and does not account for our findings.

Our findings are consistent with the sparse studies conducted among never smokers.^{1,2} Several explanations may be suggested. First, occupational exposures are more frequent among men and among the least educated groups, and may partly account for our findings.⁵ The evidence regarding other risk factors is less clearcut. The association between environmental tobacco smoke and lung cancer is modest, and this exposure is often more prevalent among women.⁶ No association has been found between vegetable consumption or body mass index and lung cancer risk among never-smokers.^{7,8} Second, the never-smoking population may exhibit different characteristics in different countries. In North America, our most-educated category is large, and due to the various stages of the smoking epidemic, there are more never-smokers among highly educated men. Consequently, highly educated never-smoking men are more selected in Europe and may exhibit a better profile, especially regarding occupational exposures.

Never-smokers are likely to differ from the general population, with a healthier lifestyle or less occupational exposures, and our results can probably not totally be extrapolated to the general population. However, we investigated inequalities among all subjects with a careful adjustment for smoking. The results were consistent with our findings among never smokers (see eAppendix, <http://links.lww.com/EDE/A833>). Our study therefore suggests that smoking may not account for all educational differences in lung cancer risk.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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TABLE

Age-Adjusted Associations of Education with Lung Cancer by Region and Source of Controls Among Never-Smokers

	Educational Level							
	High ^a		Middle			Low		
	No. Cases/ No. Controls	OR	No. Cases/ No. Controls	OR	(95% CI)	No. Cases/ No. Controls	OR	(95% CI)
Men								
All (without Spain)	229/991	1.00	123/785	0.93	(0.72–1.22)	105/486	1.35	(1.10–1.66)
Region								
Spain	8/16	1.00	4/61	0.07	(0.01–0.32)	15/305	0.05	(0.01–0.16)
France, Italy	16/310	1.00	34/485	1.38	(1.28–1.48)	29/346	1.70	(1.57–1.84)
North America	213/681	1.00	89/300	0.84	(0.63–1.12)	76/140	1.33	(1.02–1.74)
Source of controls								
Population	87/555	1.00	84/614	1.03	(0.66–1.60)	84/408	1.45	(1.06–1.98)
Hospital (without Spain)	142/436	1.00	39/171	0.82	(0.72–0.94)	21/78	1.27	(0.77–2.10)
Women								
All	338/987	1.00	386/1050	1.03	(0.91–1.17)	485/1246	1.27	(0.93–1.75)
Region ^b								
Spain, France, Italy	29/104	1.00	103/323	1.15	(0.94–1.40)	204/467	1.49	(0.89–2.50)
North America	307/866	1.00	263/641	0.99	(0.88–1.11)	129/221	1.16	(0.74–1.84)
Source of controls								
Population	160/555	1.00	243/698	0.95	(0.83–1.08)	250/527	1.15	(0.81–1.64)
Hospital	178/432	1.00	143/352	1.14	(0.91–1.42)	235/719	1.50	(0.84–2.67)

^aReference category.

^bBecause of too small numbers, we do not present the results for the study conducted in Singapore separately.