Quantifying the mediating effects of smoking and occupational exposures in the relation between education and lung cancer – the ICARE study

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Two sensitivity analyses were conducted to assess the potential residual confounding by misclassification of smoking and occupational exposures. In the first analysis (table S1), we randomly increased smoking consumption for 15% of ever smokers by selecting a higher smoking consumption value in the dataset. We left occupational exposures unchanged.In the second analysis (table S2), we randomly increased smoking consumption for 15% of ever smokers by selecting a higher smoking consumption value in the dataset. We also increased occupational exposures to asbestos and silica and to diesel motor exhaust to the immediately higher category among 5% randomly selected men.
The results suggested that possible misclassification of smoking and occupational exposures did not account for our findings. Although the indirect effects were smaller in the sensitivity analyses than in our main analyses, the main conclusions did not change. For instance, the indirect effect among primary educated men for smoking decreased from 1.35 (1.15-1.58) to 1.27 (1.09-1.47). In addition, the indirect effects for occupational exposures were not affected by smoking misclassification. Indeed, the indirect effects presented in table S1 are similar to those presented in table 3 in the article.

Table S1: Effect of misclassification of smoking:Direct and mediated effects (OR and 95% confidence intervals) of educational level on lung cancer for each mediator derived from the marginal structural models including multiple mediators. Icare 2002-2007 men.

	Primary -> Tertiary	Vocational secondary -> Tertiary	High school -> Tertiary
Smoking as mediator			
Direct effect	3.04 (2.37-3.88)	1.92 (1.55-2.36)	1.43 (1.08-1.89)
Indirect effectthrough CSI	1.27 (1.09-1.47)	1.23 (1.09-1.38)	1.15 (0.98-1.34)
Smoking and combined exposure to asbestos and silica as mediators			
Direct effect	2.38 (1.84-3.10)	1.57 (1.26-1.96)	1.26 (0.93-1.69)
Indirect effectthrough CSI	1.26 (1.09-1.46)	1.22 (1.09-1.37)	1.14 (0.98-1.33)
Indirect effect through asbestos and silica	1.23 (1.16-1.31)	1.19 (1.13-1.26)	1.06 (1.03-1.11)
Smoking, combined exposure to asbestos and silica and exposure to DME as mediators			
Direct effect	2.22 (1.70-2.92)	1.47 (1.17-1.85)	1.19 (0.88-1.60)
Indirect effectthrough CSI	1.26 (1.09-1.45)	1.22 (1.09-1.36)	1.14 (0.98-1.33)
Indirect effect through asbestos and silica	1.22 (1.15-1.30)	1.19 (1.12-1.25)	1.06 (1.02-1.10)
Indirect effectthrough DME	1.03 (1.00-1.07)	1.02 (1.00-1.05)	1.02 (1.00-1.04)

CSI: Comprehensive Smoking Index; DME: Diesel Motor Exhaust
Confidence intervals were calculated using a bootstrap resampling method with 2500 replications.

Table S2: Effect of misclassification of smoking and occupational exposures:Direct and mediated effects (OR and 95% confidence intervals) of educational level on lung cancer for each mediator derived from the marginal structural models including multiple mediators. Icare 2002-2007 men.

	Primary ->Tertiary	Vocationalsecondary ->Tertiary	High school ->Tertiary
Smoking as mediator			
Direct effect	3.04 (2.37-3.88)	1.92 (1.55-2.36)	1.43 (1.08-1.89)
Indirect effectthrough CSI	1.27 (1.09-1.47)	1.23 (1.09-1.38)	1.15 (0.98-1.34)
Smoking and combined exposure to asbestos and silica as mediators			
Direct effect	2.46 (1.90-3.18)	1.61 (1.29-2.01)	1.29 (0.95-1.73)
Indirect effectthrough CSI	1.26 (1.09-1.46)	1.22 (1.09-1.37)	1.14 (0.98-1.33)
Indirect effect through asbestos and silica	1.20 (1.13-1.28)	1.17 (1.11-1.23)	1.05 (1.02-1.10)
Smoking, combined exposure to asbestos and silica and exposure to DME as mediators			
Direct effect	2.34 (1.79-3.05)	1.53 (1.22-1.91)	1.24 (0.91-1.67)
Indirect effectthrough CSI	1.26 (1.09-1.45)	1.22 (1.09-1.37)	1.14 (0.98-1.33)
Indirect effect through asbestos and silica	1.20 (1.13-1.27)	1.16 (1.11-1.23)	1.05 (1.02-1.09)
Indirect effectthrough DME	1.02 (1.00-1.06)	1.02 (1.00-1.04)	1.01 (1.00-1.03)

CSI: Comprehensive Smoking Index; DME: Diesel Motor Exhaust
Confidence intervals were calculated using a bootstrap resampling method with 2500 replications.