

# Analysis of the joint effects of radon exposure and smoking on lung cancer risk in three nested case-control studies in Europe

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## Abstract

**Objectives:** Three case-control studies nested in the French (Fr), German (Ge) and Czech (Cz) cohorts of uranium miners were conducted in the frame of a European research Project, named Alpha-Risk, on the quantification of risks associated with multiple radiation exposures. These case-control studies aimed at assessing the effect of protracted radon exposure on lung cancer risk taking into account individual tobacco consumption.

**Material and methods:** In the three case-control studies, cases were miners of the corresponding cohort who died of lung cancer (100, 704, 672 cases for the Fr, Ge and Cz study, respectively). For each case, controls were randomly matched on birth period and attained age at the time of death of the corresponding case (500, 1398 and 1491 controls for the Fr, Ge and Cz study, respectively). Cumulated radon exposure during employment was obtained from ambient and individual measurements for the Fr and Cz studies, and from a job exposure matrix for the Ge study. Smoking habits were retrospectively determined from medical archives and questionnaires applied in face-to-face interviews, phone calls or mailings. Analysis was performed by conditional logistic regression using a linear excess relative risk (ERR) model. A multiplicative model was fitted to assess the joint effect of radon exposure and smoking on lung cancer risk.

**Results:** Smoking status was established for 62, 421, and 672 cases and 320, 620, and 1491 controls for the Fr, Ge, and Cz study, respectively. Two categories (“ever smokers” vs. “never smokers”) were defined. The percentages of “ever-smokers” were 90%, 95%, and 92% for the cases and 73%, 75%, and 73% for the controls, for the Fr, Ge and Cz study, respectively. Mean five-year lagged cumulated radon exposures were 115, 717 and 174 working level months (WLM) for the cases, and 71, 505 and 118 WLM for the controls, for the Fr, Ge and Cz study, respectively. The excess relative risk per WLM (ERR/WLM) was 0.98% with a 95% confidence interval (CI) of 0.18-3.08% for the Fr study, 0.25% (95% CI: 0.13-0.46%) for the Ge study and 1.96% (95% CI: 1.07-3.98%) for the Cz study. When adjusting for smoking, radon associated risk was still statistically significant and little modified: ERR/WLM = 0.85%, 0.23%, and 1.54% for the Fr, Ge and Cz study study. The effect of smoking on lung cancer risk was comparable to results reported in previous miners’ cohorts (odds-ratios between 3 and 7).

**Conclusions:** A consequent effort was carried out to collect smoking status for the miners included in these three nested case-control studies. This

analysis shows that the effect of radon exposure on lung cancer risk persists when smoking is taken into account. Moreover, when adjusting on smoking, the estimated lung cancer risk coefficients associated to radon exposure are close to those obtained from the corresponding cohort. In the framework of Alpha-Risk, a collaborative work including these data should allow a more powerful analysis of radon exposure and smoking effects on lung cancer risk among uranium miners.

***KEYWORDS: Epidemiology; Radon; Smoking; Uranium miners; Lung cancer.***