

Supplementary Information 1: Investigation Outline (ESM_1.pdf)

On the non-linearity of radon-induced lung cancer

Environmental Science and Pollution Research

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Aim: To investigate the risk of LC from very low-dose residential radon exposure and its modification by smoking, sex, age and histological subtype (risk-profile modification)

Design: Case-control design based on participating ILCCO studies with sufficient exposure heterogeneity.

Outcome measure: incident primary lung cancer

Exposure: mean spatial indoor-radon exposure in the surrounding area as becquerels per cubic meter [Bq/m³] based on available national or regional surveys, intended to describe regional (spatial) indoor radon exposure.

Participating studies Included case-control and cohort studies of lung cancer in USA (HSPH), Canada (MSH-PMH, I-ELCAP Toronto), Europe (CAPUA-Spain, EAGLE-Italy), and Israel (NICCC-LCA); Excluded studies: ATBC (Finland), LLP (UK), GLCS (Germany), MEC (Hawaii, USA), MDCS (Malmö, Sweden), TLC Moffitt (USA)

Results: An U-shape risk profile fits best, with the lowest risk exposure level (LRE) being at 57.6 Bq/m³ (95%-CI: 56.1-59.2 Bq/m³). A significant increase in the risk of overall-LC at 25 Bq/m³ (OR=1.31, 95%-CI: 1.01-1.59) was comparable to that at 100 Bq/m³ (OR=1.34, 95%-CI: 1.20-1.45).

Conclusion

Exposure to spatial indoor-radon is linked with lung cancer by a U-shaped profile, at very low exposure levels (sIR<200 Bq/m³). The lowest risk appears in areas of mean indoor radon levels of about 58 Bq/m³.

Risk profiles differ between histological subtypes; sex, age and smoking behaviour modify the lowest risk exposure level (LRE).

A model based on the linear non-threshold assumption (LNT) is not optimal to describe the dose-response relation of sIR lower than 200 Bq/m³.

The linearity-no-threshold assumption (LNT) is not optimal for the dose-response relation of sIR less than 200 Bq/m³.

The assignment of spatial indoor radon values (sIR) is a useful proxy for radon exposure.