RadoNorm
Managing risks from radon and NORM

Deliverable D4.1

Report on the impact of smoking on radon-associated lung cancer risk in Europe

Work Package 4

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Authors	**Ladislav Tomášek (SURO), Francesco Bochicchio (ISS), Sara Antignani (ISS), Enora Clero (ASNR), Estelle Rage (ASNR).**

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Executive Summary

Lung cancer risk from radon is closely linked to smoking. In European residential studies, the impact is assessed by stratification in logistic models of relative risk. In addition to usual demographic variables, the stratification should include smoking variables. In European residential studies, these are categories of never-, current-, and ex-smokers. The level of smoking is also characterized by number of cigarettes smoked daily and by time since quitting. The most important variable is duration of smoking or better - smoking exposure in pack-years. In European collaborative analysis of 13 studies, the last two variables were not used. This led to underestimated risk per unit radon exposure (ERR/100Bq m^{-3} = 0.084), whereas in joined Czech-French-Italian residential study with pack-years stratification, the risk per unit radon exposure was substantially higher (ERR/100Bq m^{-3} = 0.162).

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1. Evaluations of the impact of smoking on radon-associated lung cancer risk in Europe

The first studies on lung cancer and radon were conducted among uranium miners. Smoking data were not available in the earlier results and was only considered in later results when some data on smoking were available. On the other hand, the impact of smoking on radon-associated lung cancer risk is assessed in studies of residential radon (see e.g., Darby et al. 1998). In the European collaborative analysis, the logistic regression model was used where the risk (odds ratio) R was linearly dependent on exposure W. Generally, smoking impact was assessed by stratification. It was assumed that the risk is linear with cumulative radon exposure W in previous 5-34 years

$$R = R_0 (1+ b W).$$

Smoking effect in this model is included in term R_0 by stratification. The stratification scheme was analyzed quite thoroughly (Table 9, Darby et al, Scand J Work Environ Health 2006). The a priori strata included: study, age, sex, region, and smoking. The estimate of regression term b (excess relative risk per unit exposure, ERR/100Bq m^{-3}) was also formally studied in models where one of the stratification variables was omitted. In these models, all the variables (except region) were found substantial.

There were several additional strata comprising social status, occupational risk, home occupancy, and urban-rural status, but these did not bring any substantial improvement in the risk model. Further analyses were conducted for detailed description on smoking history of subjects including age when started and several categories of time since quitting.

The final stratification included the priori strata and

- age when smoking started (<15, 15-17, 18-20, 21+),
- amount smoked (<15, 15-24, 25+ cigarettes per day),
- and ex-smokers separately for time since quitting (<10 and 10+ years).

This stratification improved the risk estimate of ERR/100Bq m^{-3} from 0.052 to 0.084. The final estimate of the risk coefficient in relation to the observed residential radon is

$$\text{ERR/100Bq } m^{-3} = 0.084 \text{ (95\%CI } 0.030 – 0.158).$$

The smoking strata in this collaborative study, however, did not include one important variable – the duration of smoking nor the total amount of cigarettes (pack-years), which are known to influence substantially to the risk of lung cancer (see for instance Simonato et al, 2001, Boffetta et al. 1999). The relative risks (in terms of odds ratio) for duration of smoking is in range up to about 20, for pack-years the range is up to about 40 (Table 1 and 2). The study by Simonato et al included ten case-control studies from six European countries to investigate the major risk factors for lung cancer and included 7609 cases of lung cancer and 10431 controls. The paradox is that some of the studies (or their parts) were the studies included among European radon studies.

Table 1. Lung cancer risk in European case-control studies (Simonato et al 2001) by categories of pack-years.

	Men				Women			
Pack-years	Cases	Controls	OR	95%CI	Cases	Controls	OR	95%CI
Non-smokers	117	1750	1.00		443	1337	1.00	
<20	588	754	11.04	(8.87–13.74)	213	197	3.45	(2.73–4.36)
20–29	688	509	18.17	(14.54–22.70)	176	67	8.81	(6.42–12.08)
30–39	874	410	27.91	(22.30–34.94)	153	28	18.09	(11.82–27.68)
40+	1683	687	37.08	(29.99–45.85)	187	33	19.61	(13.22–29.08)

Table 2. Lung cancer risk in European case-control studies (Simonato et al 2001) by categories of duration of smoking.

	Men				Women			
Duration	Cases	Controls	OR	95%CI	Cases	Controls	OR	95%CI
Never + <20 y	312	2886	1.0		555	1601	1.0	
20–29 y	663	1059	5.0	(4.3–5.8)	218	144	4.3	(3.3–5.5)
30–39y	1666	1385	11.0	(9.6–12.7)	288	123	7.2	(5.6–9.1)
40y +	3000	1923	21.6	(18.6–24.9)	274	99	8.6	(6.6–11.3)

The present model of the risk implicitly in term R_0 assumes multiplicative interaction. When it is expressed explicitly

$$R = R_0 (1+ c S) (1+ b W).$$

The models in task 4.1 are more general geometric mixture models. The European residential model (Darby et al 2006) described above can be directly compared with estimates from the Czech, French, and Italian residential studies in Milestone 54 for multiplicative smoking-radon interaction (mixing parameter Θ=1), where the estimates are

$$ERR/100Bq\ m^{-3} = 0.162\ (90\%CI\ 0.096 – 0.276),$$

$$ERR/PKY = 0.214\ (90\%CI\ 0.171 – 0.269).$$

Although the combined study from the Czech Republic, France and Italy in Milestone 54 (1250 cases, 2381 controls) is only a part of the European collaborative study (7148 cases, 14 208 controls), the difference in the risk coefficients (European vs task 4.1) is remarkable.

For comparison, in combined North America studies (Krewski et al 2006), the stratification included:

- study, sex, age,
- number of cigarettes smoked per day,
- duration of cigarette smoking,
- years since stopping cigarette smoking,
- number of residences,
- years with α-track measurements.

The estimate of the risk coefficient from this combined study (4004 cases, 5155 controls) was

ERR/100Bq m^{-3} = 0.09 (95%CI -0.01 – 0.26).

2. Conclusion

In European residential studies, the impact is assessed by stratification in logistic models of relative risk. In addition to usual demographic variables, the stratification should include smoking variables. The most important variable is duration of smoking or better - smoking exposure in pack-years. In European collaborative analysis of 13 studies, the last two variables were not used. This led to underestimated risk per unit radon exposure (ERR/100Bq m^{-3} = 0.084), whereas in the joined Czech-French-Italian residential study with pack-years stratification, the risk per unit radon exposure was substantially higher (ERR/100Bq m^{-3} = 0.162).

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