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Lung cancer mortality and radon exposure in Russia

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Abstract. The association between the lung cancer and indoor radon exposure in Russian population was investigated. The average indoor radon concentration for each region was estimated using the annual reports issued by the Saint-Petersburg Ramzaev Research Institute of Radiation Hygiene for the period 2008–2013. The average standardized lung cancer mortalities among males and females were estimated using the reports of the Moscow Hertzen Cancer Research Institute for the period 2008–2012. The relative risk (RR) was estimated as a ratio between the average mortality within seven exposure intervals and background mortality. The slope factors of linear dependence between the indoor radon exposure and lung cancer RR are 0.026 (–0.11÷0.17) and 0.83 (0.52–1.12) per radon concentration 100 Bq/m^3 for males and females, respectively (with 90% confidence interval). The obtained results can be explained by the confounding effect of tobacco smoking. Significant excess risk of lung cancer in female population can be associated with radon exposure and low prevalence of smoking.

Key words: lung cancer • radon • relative risk • smoking

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Introduction

Cohort studies of uranium miners and case control studies of indoor radon and lung cancer conducted in the recent decades have provided strong evidence that radon exposure causes lung cancer [1]. The epidemiological observations of uranium miners in the 1980s and 1990s revealed lung cancer as the main health effect associated with radon progeny inhalation. According to the joint analysis of 11 cohort studies performed by Lubin *et al.* [2], the risk of lung cancer depends on the radon exposure with regard to either rate of exposure or duration of exposure the following factors modify the risk as well: sex, time since exposure, age at the beginning of exposure, and attained age. A comparison of detriment due to radon exposure of miners with known health effects of whole body external exposure (life-span study of A-bomb survivors [3] and other studies) was applied to estimate the dose coefficient using the conversion convection [4]. While the findings of miners' cohort studies were obtained for an exposure range higher than the indoor radon levels, radon-induced risks for population were estimated by extrapolation of miners data to the range of low radon concentration.

Later, a case-control design of the epidemiological analysis was applied to investigate lung cancer risks due to indoor radon exposure. The main advantages of case-control and cohort studies are as follows:

- individual data on radon exposure (both concentration and duration),
- individual data on smoking,
- individual data on other carcinogens,
- possibility to perform meta-analysis and pooling analysis.

At the same, it appeared that a single case-control residential study has insufficient statistical power to obtain reliable results on the risk of radon-induced health effects. The point estimates of excess relative risk (ERR) of lung cancer were both negative and positive in different studies, while 95% confidential intervals included negative and positive values in all studies. However, the meta-analyses of published data have produced significant ERR >1 at a relatively low indoor radon concentration [5–7]. The most reliable data on lung cancer risk associated with indoor radon were gained after pooling analysis of residential studies, which utilizes the advantages of case-control type of study and provides higher statistical power. According to the pooling of European residential case-control studies, ERR = 1.16 (95% confidence interval 1.05–1.31) at radon concentration 100 Bq/m^3 [8]. Basing on the pooling analyses of residential studies in Europe and Northern America [9], WHO concluded that radon is second after smoking cause of lung cancer in general population [10]. ICRP considered these results as reliable arguments for justification of protection strategy and a basis for establishing the national-derived reference levels of the indoor radon concentration below 300 Bq/m^3 [1, 11].

Another type of study of the dose-effect relationship is ecological or geographical correlation one. This type is cheap and rapid. It allows generalization, exploration of time trends, and generating of hypothesis. But, there are strong limitations associated with the aggregated data. The use of standard epidemiological precautions is necessary when interpreting the results of the ecological study.

The most cited ecological study was conducted by Cohen in the USA [12]. Cohen estimated the correlation between the average indoor radon concentration and lung cancer mortality in 1601 USA counties and found a strong negative dependence. The findings of this study that contradict to the dose-effect relationship observed among the miners provoked remarkable scientific discussion. Most of specialists criticized the design of ecological study, which is unable to account for individual smoking status [7, 13]. Thoroughly evaluating all epidemiological data, UNSCEAR and ICRP concluded that there is a strong scientific base to apply linear non-threshold dependence (LNTD) for lung cancer risk and indoor radon exposure [1, 7].

In the last decades in Russia, considerable progress was achieved in indoor radon measurements. The measurements of radon concentration at homes are conducted in most of regions of the country. More than 400 measurements are performed in the half of the 83 regions annually. The total number of indoor radon EEC measurements amounts to several hundreds of thousands. The level of medical care ensures reliable diagnosing of lung cancer cases and medical statistic recording as well. Thus, it is possible to compare lung cancer mortality and indoor radon by regions of Russia, using the ecological design study. Such analysis is not intended to test LNTD, while individual control of smoking could not be enabled. On the contrary, the aim is to investigate the confounding effect of smoking in the ecological study. The results of the ecological study in Russia are compared with the results of pooling analysis of European residential case-control studies as well.

Materials and methods

The average indoor radon concentration in each region of Russia was reconstructed basing on the data in the Integrated State System for Doses Control and Registration – so-called Form DOZ Number 4. This form is included in the annual reports issued by the Saint-Petersburg Institute of Radiation Hygiene [14–19]. An annual report for each region provides the value of average indoor radon equilibrium equivalent concentration and the number of measurements by three main type of buildings: wooden house, one-storey stone house (constructed using stone, brick, concrete, and so on), and multi-storey stone house. Totally, information of more than 400 000 measurements of indoor radon equivalent equilibrium concentration in 83 regions of Russia was used. The standardization of radon measurements is ensured by meeting the requirements of the state metrological system. According to the estimations, the radon concentration lies in the range from 20 to 80 Bq/m^3 in most of the regions, and the average indoor radon concentration in Russia is 48 Bq/m^3. In more detail, the approach to reconstruction of national distribution of indoor radon concentration in Russia is presented in [20]. The regional average radon concentrations are presented in Table 1 and their distribution is shown in Fig. 1.

Information on malignant neoplasm in Russia is collected by the Moscow Hertzen Cancer Research Institute, which issues its reports annually as well [21–25]. The regional 5-year average standardized lung cancer mortality of females and males is presented in Table 1 and its distribution is shown in

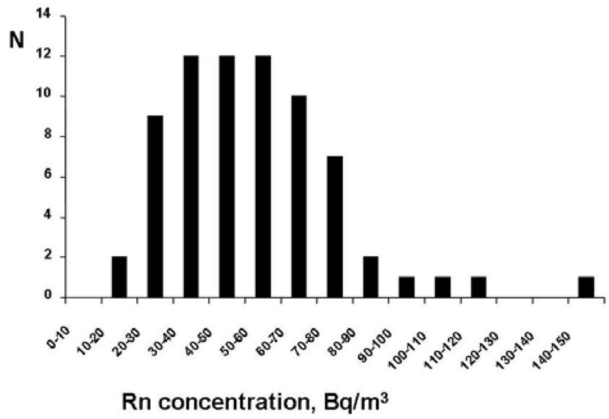

Fig. 1. Distribution of the regional average radon concentration.

Table 1. Average indoor radon concentration (Rn) and average lung cancer mortality (M) per 100 000 in the regions of Russia

Region	Rn [Bq/m^3]	M		Region	Rn [Bq/m^3]	M	
		Male	Female			Male	Female
Adygea	128	50.812	5.454	Murmansk Oblast	54	48.534	5.378
Altai Krai	72	66.892	6.302	Nizhny Novgorod Oblast	71	48.652	3.964
Amur Oblast	81	55.368	6.424	Novgorod Oblast	44	55.596	4.726
Arhangelsk Oblast	41	57.398	5.008	Novosibirsk Oblast	65	57.852	6.436
Astrakhan Oblast	26	57.718	4.962	Omsk Oblast	70	61.094	6.146
Bashkortostan	72	39.012	3.878	Orenburg Oblast	64	61.002	5.608
Belgorod Oblast	76	43.580	4.828	Oryol Oblast	35	53.334	5.408
Bryansk Oblast	32	50.552	4.458	Penza Oblast	47	47.768	4.536
Buryatia	119	50.238	9.220	Perm Krai	62	49.576	4.936
Chechnya	29	47.616	7.210	Primorsky Krai	57	57.564	8.310
Chelyabinsk Oblast	79	56.220	6.034	Pskov Oblast	72	56.094	4.604
Chuvashia	65	41.684	5.424	Rostov Oblast	76	48.946	5.496
Irkutsk Oblast	92	56.398	7.406	Ryazan Oblast	77	51.760	5.126
Ivanovo Oblast	82	52.358	3.936	Samara Oblast	46	47.286	5.060
Jewish Autonomous Oblast	146	67.206	8.192	Saratov Oblast	57	45.342	4.654
Kaliningrad Oblast	47	41.856	5.706	St. Petersburg	61	41.108	7.004
Kalmykia	109	48.774	6.858	Sverdlovsk Oblast	95	58.682	5.350
Kaluga Oblast	84	48.832	4.740	Smolensk Oblast	38	45.522	4.366
Karachay-Cherkessia	99	42.388	4.600	Stavropol Oblast	101	44.392	5.092
Karelia	73	62.506	4.942	Tambov Oblast	62	53.326	5.326
Kemerovo Oblast	88	60.756	6.630	Tatarstan	58	41.758	4.874
Khabarovsk Krai	63	59.646	7.862	Tomsk Oblast	43	57.700	7.606
Khakassia	59	60.022	6.898	Tula Oblast	63	50.754	5.238
Kirov Oblast	61	50.228	4.322	Tuva	177	51.082	9.098
Kostroma Oblast	54	52.170	3.638	Tver Oblast	37	53.746	4.568
Krasnodar Krai	96	45.274	5.830	Udmurtia	41	46.584	4.738
Krasnoyarsk Krai	37	63.860	8.848	Ulyanovsk Oblast	24	52.164	4.570
Kurgan Oblast	78	68.862	6.552	Vladimir Oblast	47	54.602	4.812
Kursk Oblast	46	53.300	6.172	Volgograd Oblast	37	51.606	5.320
Leningrad Oblast	79	51.030	6.036	Vologda Oblast	54	52.510	4.308
Lipetsk Oblast	56	47.618	4.690	Voronezh Oblast	35	44.974	4.788
Mari El	21	48.592	3.550	Yakutia	66	46.240	12.500
Mordovia	33	48.512	4.838	Yaroslavl Oblast	75	51.380	4.298
Moscow Oblast	88	44.008	5.788	Zabaykalsky Krai	230	54.646	10.400

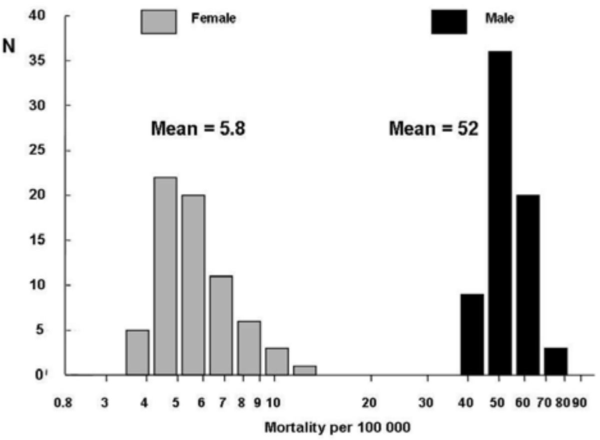

Fig. 2. Distribution of the regional annual lung cancer mortality.

Fig. 2. The difference between males and females is large – order of magnitude. The mean value is 52 per 100 000 males and 5.8 per 100 000 females.

Due to remarkable climatic and socio-economic inconsistency with other regions of Russia, some arctic regions, mountain regions, and capital city were excluded from the analysis: Dagestan, Kamchatka Krai, Altai Republic, Komi Republic, Sakhalin Oblast, North Ossetia, Tyumen Oblast, Khanty-Mansi Autonomous Okrug, Chukotka Autonomous Okrug, Yamalo-Nenets Autonomous Okrug, Magadan Oblast, and Moscow.

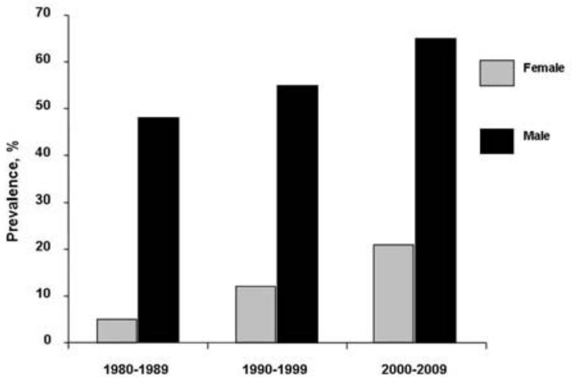

Fig. 3. Tobacco use prevalence in Russia according to [26].

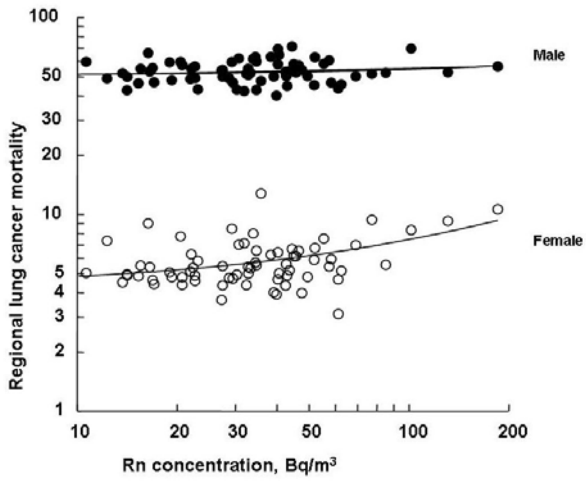

Fig. 4. The regional lung cancer mortality vs. the average regional radon concentration.

Information of tobacco smoking in the Russian population was obtained from the results of the Global Adult Tobacco Survey [26] conducted in Russia in 2009. The tobacco use prevalence in Russia in periods 1980–1989, 1990–1999, 2000–2009 for males and females are presented in Fig. 3.

The relative risk (RR) of lung cancer was estimated as a ratio between the observed mortality and mortality expected for zero indoor radon concentration. To analyse the dependence of ERR = RR-1 on exposure, the regional indoor radon concentration estimated using an equilibrium factor 0.4 were divided into seven intervals: <37, 37–46, 47–58, 59–65, 66–76, 77–95, and >95 Bq/m^3. Each interval contains 8–10 values.

Results

Dependences between 5-year average lung cancer mortalities among males and females and the regional average indoor radon concentration are presented in Fig. 4. A simple linear model is applied to fit the observed relationship:

$$M(Rn) = M_0 + b \cdot Rn,$$

where, M(Rn) is the observed mortality (per 10^5) at the indoor radon concentration Rn [Bq/m^3]; M_0 is the intercept factor equal to mortality at Rn = 0 (per 10^5); b is the slope factor of linear dependence, $10^{-4}/(Bq/m^3)$.

A positive significant correlation between the indoor radon and lung cancer was found for the female population, while for males, it appeared insignificant (Table 2).

For further analysis, we estimated the RR as a ratio between the observed mortality and mortality estimated for zero indoor radon concentration ($RR = M/M_0$). The estimated values of RR for seven intervals of the indoor radon concentrations with 90% confidence interval are presented in Fig. 5 for females and males, respectively. The 90% confidence interval for RR is estimated taking into account both variation of M within the intervals of the radon concentration and M_0. The dependence of RR on the average indoor radon concentration in the intervals is fitted using the following model equation:

$$RR = 1 + B \cdot Rn,$$

where, the risk coefficient B = 0.52 (0.27–0.77) per 100 Bq/m^3 and 0.03 (–0.06÷0.13) per 100 Bq/m^3 for females and males, respectively (with 90% confidence intervals).

Table 2. Coefficients of linear regression between the regional lung cancer mortality and the average regional indoor radon concentration

	M_0	$b \cdot 100$ [Bq/m^3]
Male	50 ± 4	2.1 ± 5.7
Female	4.3 ± 0.7	2.4 ± 1.2

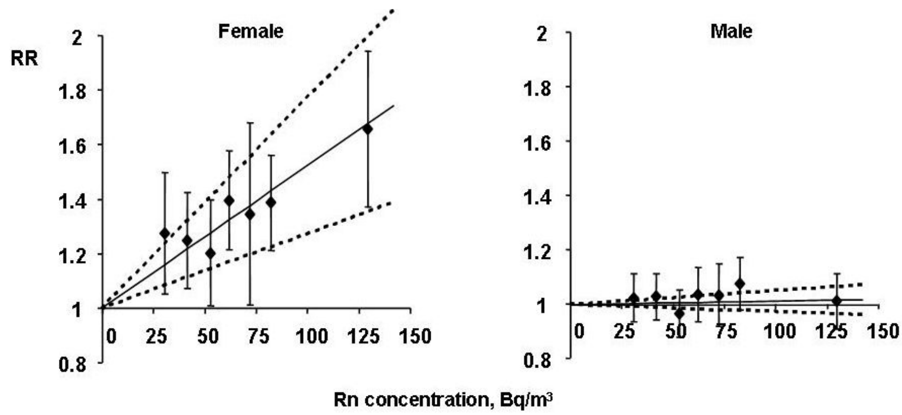

Fig. 5. Relative risk vs. radon concentration.

Discussion

The results of the ecological study should be analysed taking into account the confounding effect of tobacco smoking. To analyse the influence of smoking, we applied the results of the Global Adult Tobacco Survey [26] conducted in Russia in 2009 (Fig. 3). As can be seen in the figure, the prevalence of smoking among males is very high – above 50%. Female smoking rises during 30 years from 5 to 20%. It is necessary to note that 20 years before 2009, the smoking prevalence among women was relatively low in Russia.

We suppose that the risk of lung cancer induced by indoor radon exposure can be hidden behind the confounding effect of tobacco smoking. Consequently, a possibility to obtain significant RR associated with radon is higher when tobacco smoking is lower. The effect of radon exposure in females appears under low prevalence of the smoking in the Russian female population 20 years before. Taking into account 10–20 years latent period for lung cancer, the contribution of smoking to female lung cancer mortality in Russia in period from 2009 to 2012 is expected to be low by an absolute value and considerably lower than the contribution to the lung cancer mortality in males. The effect of radon exposure of male population of Russia cannot be found due to the high level of tobacco smoking between males.

The results of the geographical correlated analysis of indoor radon and lung cancer in the Russian regions are compared with the pooling of European case-control study performed by Sarah Darby with colleagues [8]. Figure 6 shows the estimations of ERR per 100 Bq/m^3 obtained in the pooling analysis for all persons – mixture of smokers and non-smokers, and our results for females and males. The tendency for higher radon-induced risk for low-smoking population can be suggested from the comparison of Russian female data and European mixture population. It may result in underestimation of risk for the low-smoking population. The higher value of ERR for Russian female low smoking population may relate to different radon-induced ERR for smokers and non-smokers. The results of ERR estimations for smokers in the European pooling study and for high-smoking Russian males can be considered similar. However, the central estimation of ERR in European pooling is higher that can be associated with the application of individual data on smoking in the analysis.

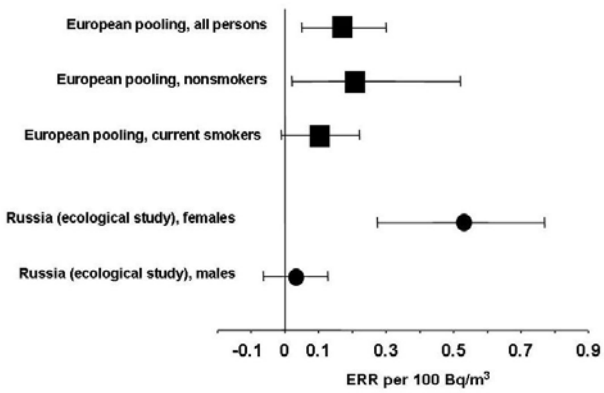

Fig. 6. Excess RR per 100 Bq/m^3 (European pooling – after correction for uncertainties [8]).

Comparing ERR obtained in the European poling for mixture of males and females, smokers and non-smokers, and the result of ecological study in Russia suggests that ERR from the pooling analysis of case-control studies can be accepted for radon risk estimations in Russia. Such estimation is necessary for justification of protection against radon exposure at home.

Conclusion

The general conclusions of the study are as follows:
- Assessment of lung cancer risk induction due to indoor radon exposure in Russia can be based on the results of pooled analysis of European case-control studies.
- Unusual proportion of smokers and non-smokers in male and female population is a significant source of uncertainty for risk projection.
- Interaction with smoking is still a challenging research task.

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