CHRISTINA SØYLAND HASSFJELL

Norwegian Radiation Protection Authority

TOM KRISTIAN GRIMSRUD

Research Department Cancer Registry of Norway

WILLIAM J.F. STANDRING

william.standring@nrpa.no Norwegian Radiation Protection Authority

STEINAR TRETLI

Research Department Cancer Registry of Norway

Lung cancer prevalence associated with radon exposure in Norwegian homes

BACKGROUND

Radioactive radon gas is generated from uranium and thorium in underlying rocks and seeps into buildings. The gas and its decay products emit carcinogenic radiation and are regarded as the second most important risk factor for lung cancer after active tobacco smoking. The average radon concentration in Norwegian homes is higher than in most other Western countries. From a health and cost perspective, it is important to be able to quantify the risk of lung cancer posed by radon exposure.

MATERIAL AND METHOD

We estimated the radon-related risk of lung cancer in Norway based on risk estimates from the largest pooled analysis of European case-control studies, combined with the hitherto largest set of data on radon concentration measurements in Norwegian homes.

RESULTS

Based on these estimates, we calculate that radon is a contributory factor in 12% of all cases of lung cancer annually, assuming an average radon concentration of 88 Bq/m³ in Norwegian homes. For 2015, this accounted for 373 cases of lung cancer, with an approximate 95% confidence interval of 145–682.

INTERPRETATION

Radon most likely contributes to a considerable number of cases of lung cancer. Since most cases of radon-associated lung cancer involve smokers or former smokers, a reduction of the radon concentration in homes could be a key measure to reduce the risk, especially for persons who are unable to quit smoking. The uncertainty in the estimated number of radon-associated cases can be reduced through a new national radon mapping study with an improved design.

MAIN MESSAGE

Estimates based on data from 2001 showed that radon was a contributory factor in approximately 12% of all cases of lung cancer in Norway in 2015

Relatively simple measures to reduce the amount of residential radon may reduce the prevalence of lung cancer by approximately 100 cases per year

Measures to reduce radon result in a greater reduction of risk for smokers and former smokers compared to those who have never smoked

ung cancer is the form of cancer that claims the highest number of lives (1). Incidence in Norway, measured as an age-standardised rate, is slightly declining for men and increasing for women (1). In 2015, altogether 1 564 cases of lung cancer were diagnosed in men and 1 471 in women. The main factor affecting the risk of lung cancer is previous and current smoking habits. There is international agreement that exposure to residential radon also accounts for an increased risk of lung cancer among smokers and non-smokers alike (2–8).

Radon is a radioactive inert gas that decays to short-lived radionuclides. The gas is generated from uranium and thorium in underlying rocks. Cracks and fissures in the bedrock and foundations cause radon to seep into buildings (2). Domestic heating in the winter season causes negative pressure in basements/lower ground floors indoors (a chimney effect). This increases the inflow of radon, while reduced ventilation and well insulated buildings help concentrate radon in the indoor air. When radon gas is inhaled, the surfaces of the airways and lungs are irradiated by alpha particles (2).

From a health and cost perspective it is important to know the extent to which lung cancer can be attributed to radon exposure. Changes in smoking habits, which vary as a function of time, geography and gender, complicate the measurement of the direct effect of anti-radon interventions. We are dependent on model estimates to undertake cost-benefit analyses of different mitigation measures. The objective of this study is to estimate the incidence of radon-associated lung cancer in Norway.

Material and method

Our estimates are based on the results from a dose-response model published by Darby and collaborators (5). They used data from 13 European case-control studies, each with at least 150 individuals with lung cancer and 150 control persons, a detailed smoking history for each individual and the measured radon concentration in their homes over the last 15 years or longer. Demographic information and individual data concerning other exposures that could affect the risk of lung cancer were also included in the data set.

Studies of miners have shown that the most relevant period for radon exposure is the interval from 34 years to five years prior to the time of diagnosis (alternatively death from lung cancer) (9). A time-weighted mean value for radon concentration in the residential homes was therefore estimated for each individual – 7 148 with lung cancer and 14 208 control persons. The average radon concentration was 104 Bq/m³ for the lung cancer patients and 97 Bq/m³ for the control persons.

Darby and collaborators used a linear model to estimate the radon-associated relative risk expressed as $RR = 1 + \beta x$, where 'x' means the long-term average radon concentration in a given residential home. They used two different measures for this radon concentration (x): a directly *observed* value and a value that was *corrected* for random variation based on data from the 13 studies included. On average, the corrected values were lower (averages of 90 Bq/m³ and 86 Bq/m³ for the lung cancer patients and the control persons respectively).

Their analyses were performed while controlling for potentially confounding factors, such as study affiliation, age, gender, region of residence and smoking history. They found the difference quotient β = 0.16 (95% confidence interval (CI) 0.05–0.31) for each increase

of 100 Bq/m³ in the corrected long-term average radon concentration. The β quotient showed no correlation with study, age, gender or smoking status. The analysis was repeated – restricted to individuals who had lived in homes with an average corrected radon concentration < 200 Bq/m³ – and β remained significantly higher than zero (p = 0.04).

They found no lower threshold value where the lung cancer risk was unaffected by the radon concentration measured in the home. The relative risk of living with a given radon concentration was independent of smoking history, but as expected, smoking was associated with a strongly increased risk of lung cancer. For men who smoked 15–25 cigarettes per day, the lung cancer risk was 25.8 (95% CI 21.3–31.2) times higher than for male neversmokers. The equivalent figures for women were 11.4 (95% CI 9.0–14.5).

Darby and collaborators assumed that an absolute cumulative risk of lung cancer (i.e. the proportion afflicted) up to the age of 75 in never-smokers with no exposure to radon amounted to 0.41%, and that the equivalent absolute risk among heavy smokers (lifelong smokers of 15–24 cigarettes per day) amounted to 10.1%. The estimates showed that these cumulative risks from living in a home with a radon concentration of 100 Bq/m³ increased to 0.47% (95% CI 0.43–0.54) for never-smokers and to 11.63% (95% CI 10.6–13.0) for heavy smokers, and at 800 Bq/m³ to 0.93% (95% CI 0.57–1.42) and 21.6% (95% CI 13.9–31.0) respectively.

For the estimates in our study we have chosen to use the hitherto largest data set of radon measurements taken in Norwegian homes (10). The measurements have been corrected to estimate the true long-term average radon concentrations in these homes (11). The mapping showed an approximately log-normal distribution of the corrected radon va-

 $\textbf{Table 1} \ \textbf{Radon measurements and distribution in selected municipalities/residential areas (10)}$

	Propor- tion of	Average radon concen- tration (Bq/m³)	The 5 highest measurements in each area, ranked (Bq/m³)				
	homes > 200 Bq/m³ (%)		no. 1	no. 2	no. 3	no. 4	no. 5
Oslo	13	102	1 000	750	690	640	610
Røyken municipality	17	154	1 500	1 500	1 500	1 400	1 100
Stange municipality	45	350	5 300	4 900	4 800	4 500	3 400
Kinsarvik (rural)	100	2 830	16 600	13 000	8 350	8 200	7 900

lues, with a national average value of 88 Bq/m 3 (95% CI 66–117) (12). The frequency distribution of the mapping data is shown in Figure 1 (3, 10), and examples of the variation in the measurements of radon concentrations from selected areas are shown in Table 1 (10).

In most cases, radon concentrations can be reduced by relatively simple methods, for example by sealing leakage points from the underlying bedrock or improving ventilation (2). Measurements taken before and after ordinary radon mitigation methods in existing homes show a halving of the radon concentration on average. More comprehensive interventions may yield far greater reductions in the radon level (2, 13). The Norwegian Radiation Protection Authority recommends that measures be taken to reduce the radon level in homes with a radon concentration of more than 100 Bq/m³ on average over the year, pursuant to Section 6, fifth paragraph, of the Radiation Protection Regulations.

In our study we used the results from Darby and collaborators to estimate the radon-associated risk of lung cancer expressed as a function of the average long-term radon concentration in Norwegian homes, hereafter referred to as $\overline{X_N}$. As our basis we used their general expression of relative risk as a function of the radon concentration, $RR(x) = 1 + \beta x$, where 'x' again denotes the radon concentration. We chose to use the value given by Darby and collaborators of $\beta = 0.16$ per 100 Bq/m³, because our radon data also include corrected long-term average radon concentrations in Norwegian homes.

In the following, N_{radon} is used as a symbol for the lung cancer incidence (the number of new cases of lung cancer per year in Norway) that has radon as a contributory factor, given that the population is living in an average radon concentration of $\overline{X_N}$ in their homes. N_{total} is defined as the total incidence of lung cancer in the same period. The radon-induced relative risk in the population can thus be expressed as

$$\begin{split} RR(\overline{X_N}) &= \frac{risk\ of\ lung\ cancer\ (radon\ concentration)\ \overline{X_N})}{risk\ of\ lung\ cancer\ (no\ radon\ exposure)} \\ &= \frac{N_{total}}{N_{total} - N_{radon}} \\ &\text{rewritten\ as} \\ &\Rightarrow N_{radon} = N_{total} \left(\frac{RR(\overline{X_N}) - 1}{RR(\overline{X_N})}\right) = N_{total} \left(\frac{\beta\overline{X_N}}{1 + \beta\overline{X_N}}\right) \end{split}$$

 $N_{\rm radon}/N_{\rm total}$ corresponds to the epidemiological concept of attributable risk (or attributable proportion) in the population (14), the percentage of cancer cases that would have been avoided in the absence of the exposure

in question, all else being equal. The attributable proportion can be estimated (14) based on relative risk using the formula (RR-1)/RR, which here is equal to $\beta/\overline{X_N}$ (1+ $\beta \overline{X_N}$) = N_{radon}/N_{notal}

The uncertainty of N_{radon} will depend on the uncertainty in the ratio N_{radon} / N_{total} , to which uncertainty in both β and \overline{X}_N contribute. A 95% CI for β = 0.16 per 100 Bq/m³ has been stated by Darby and collaborators as 0.05–0.31 per 100 Bq/m³. A 95% CI for \overline{X}_N = 88 Bq/m³ was estimated as 66–117 Bq/m³ (12). As a measure of

the total uncertainty (of β), we estimated an approximate 95% confidence interval by performing a simulation, in which we estimated the attributable proportion one million times on the basis of randomly drawn values for radon concentration (drawn within a lognormal distribution with an expected value ln(88)) and correspondingly randomly drawn values of β (drawn within an assumed normally distributed square-root transformation of β with an expected value of $\sqrt{0.16}$.

We also estimated the effect of ordinary ra-

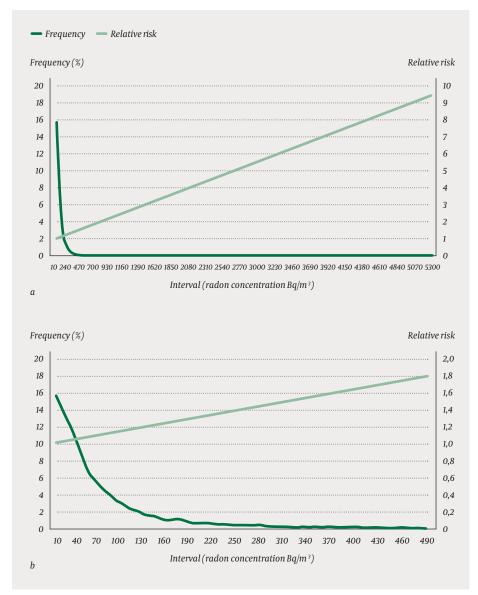


Figure 1 a) Frequency distribution of different radon concentrations in Norwegian homes (left axis, dark green curve) and estimated relative risk (RR) of lung cancer (right axis, light green curve) as a function of radon concentration in Norwegian homes (the x-axis) in the nationwide mapping undertaken in 2000–01(3, 10) – the entire data set (assuming a linear risk increase also above 800 Bq/m3). b) Frequency distribution of different radon concentrations in Norwegian homes (left axis, dark green curve) and estimated relative risk (RR) of lung cancer (right axis, light green curve) as a function of the radon concentration in Norwegian homes (the x-axis) in the nationwide mapping undertaken in 2000–01(3, 10) – only homes with a radon concentration of 0–500 Bq/m³.

don mitigation measures on the national average radon concentration and the corresponding proportion of cases of lung cancer cases that would then be attributed to radon exposure.

Results

 $RR \, \overline{X_N} = 1 + \beta \, \overline{X_N}$ where $\beta = 0.16$ per 100 Bq/m³ and $\overline{X_N} = 88$ Bq/m³ give a relative risk RR = 1.14. This means that the given radon exposure for the population as a whole will entail a 14% increase in the risk of lung cancer, when compared to a hypothetical situation of no exposure to radon and otherwise identical exposure to other lung carcinogens. Since $N_{radon} / N_{total} = \beta \, \overline{X_N} / (1 + \beta \, \overline{X_N}) = (RR - 1) / RR = (1.14 - 1) / 1.14$, the attributable proportion will amount to 12.3%, i.e. $N_{radon} = 0.123 \cdot N_{total}$

to 12.3%, i.e. $N_{radon} = 0.123 \cdot N_{total}$. I 2015, a total of $N_{total} = 3$ 035 new cases of lung cancer were diagnosed in Norway (1). The estimated number of annual cases of lung cancer for which radon is a contributory factor is thus $N_{radon} = 373$. An approximate 95% confidence interval for this number is 145–682.

Furthermore, we estimated the effect on the average radon concentration in Norwegian homes should the prevailing recommendations from the Norwegian Radiation Protection Authority on radon mitigation measures be implemented in all homes with a radon concentration above the intervention threshold of 100 Bg/m³ on average over the year. Measures to reduce the radon concentration by 50% would reduce the average level in Norwegian homes from 88 Bq/m3 (95% CI 66-117) to 59 Bq/m³ (95% CI 44-79) (Table 2). With an approximate confidence interval estimated in the same way as for the main result above, such a reduction in radon levels would give an expected reduction in lung cancer incidence from N_{radon} = 373 (approximate 95% CI

145–682) to 262 (approximate 95% CI 99–495) cases per year, i.e. around 110 fewer cases of lung cancer per year.

In the mapping study from 2001, altogether 0.18% of the homes had a radon concentration > 1 000 Bq/m³ (10). Given a linear association also at levels > 800 Bq/m³, an assumption which is supported by the high radon risks found in mines, such radon levels will pose a significant absolute risk (cumulative risk) of lung cancer for smokers, since the relative risk is estimated to be more than twice as high as in a home with no radon.

Discussion

On the basis of risk estimates for lung cancer caused by radon exposure in homes from the largest European pooled analysis published and the largest available study of radon concentrations in Norwegian homes, we calculated that radon is a contributing factor in 373 new cases of lung cancer in Norway annually (approximate 95% CI 145–682). Although this point estimate contains a lot of uncertainty, it must be regarded as the best estimate available in light of existing knowledge.

Approximately one-third of the radon-associated lung cancers are expected to be preventable by undertaking nationwide, standard radon mitigation measures in those homes that have a radon concentration above the intervention threshold defined by the Norwegian Radiation Protection Authority of 100 Bg/ m³ (2). Similar results were recently presented in Sweden (15). Requirements for a safe radon concentration in indoor air, with an intervention threshold of 100 Bq/m3 in schools, daycare facilities and rental flats, are stipulated in the current Norwegian Radiation Protection Regulations. A further reduction of radon concentrations can be achieved through preventive radon measures in the construction of new housing. Such measures are currently mandatory under Section 13–5 of the Building Code (16).

The average radon concentration of 88 Bq/m³ in Norway is higher than the average for many Western countries. The average for the 29 OECD countries is 67 Bq/m³, and the world average is reported to be 39 Bq/m³ (2). The differences are partly due to geological and climatic conditions, and partly to forms of housing and building traditions in Norway. In the period 1980–2000, the radon concentration in the housing mass increased by approximately 70% (8). Future mapping studies will be able to reveal whether new requirements for energy saving and construction techniques (16) have changed the radon concentration in Norwegian homes.

A number of mapping studies of residential radon concentrations have been undertaken in Norway, with different weaknesses and measurement procedures. The radon mapping data that we have used for this study (10) constitute the largest available Norwegian data material currently available. The uncertainty in this mapping is mainly associated with the sample of homes. A total of 114 out of 430 municipalities participated, but the sample of municipalities and homes was based on voluntary participation and was not randomly drawn. This resulted in an overrepresentation of detached and semi-detached houses compared to flats on higher floors, for example, which may have resulted in an exaggerated estimate of the average radon concentration for the population as a whole.

The mapping study from 2001 used measurements taken over two months during the winter season, corrected by a factor of 0.75 (11). This correction is to compensate for observed variations in radon measurements over time, which may be caused by ventilation conditions, meteorological factors and heating habits (2). Such elements of uncertainty can be eliminated in future mapping studies by using modern technology that permits continuous electronic registration of radon concentrations over many years in a random sample of housing units. Given that our estimates were made on the basis of a relatively old data set, new measurements would obviously also be able to produce more updated estimates of radon-associated lung cancer.

Lung cancer is primarily caused by smoking. The attributable proportion caused by tobacco amounts to 80–90%, given the smoking habits that have prevailed in Norway until today (17). Darby and collaborators showed that smoking and radon exposure in-

 $\textbf{Table 2}\ \ Distribution\ of\ average\ radon\ concentrations\ in\ Norwegian\ homes\ and\ the\ expected\ effect\ (a\ halving)\ of\ the\ radon\ concentration\ after\ standard\ radon\ mitigation\ measures\ have\ been\ taken\ (2)$

Radon con- centration (Bq/m³)	Proportion of the homes (%)	Average radon concentration in the homes (Bq/m³)	Average radon concentration in the homes after mitigation measures (Bq/m³)	New average radon concentration in the homes after mitigation measures (Bq/m³)
0-100	73	40	40 (no interventions)	59
100-200	18	144	77	
> 200	9	356	178	

crease the risk of lung cancer independently of each other, so that in combination they may result in a considerably increased absolute risk. Those 12% of the cases of lung cancer that are attributed to radon will therefore largely involve smokers and former smokers. In this context, radon can be understood as the extra influence that triggers disease.

If the number of cases of lung cancer in Norway is reduced because of changes in smoking habits, the number of radon-induced cases will also be reduced, even if the radon concentrations in Norwegian homes remain unchanged. Conversely, an elimination of radon in all Norwegian homes in the long term will result in a significant reduction in the prevalence of lung cancer (12%), even in the face of unchanged smoking habits.

The radon concentrations in Norwegian homes are log-normally distributed. Figure 1 shows that most of us live in houses with low and moderate radon concentrations, while the risk of lung cancer rises linearly as a function of the radon concentration. This implies that most radon-associated cases of lung cancer occur at low radon concentrations, while the individual risk may be considerable for the relatively few people who live in housing with high radon concentrations, and for smokers in particular.

A health benefit can be realised by reducing the highest radon concentrations (the highrisk strategy) as well as by reducing moderate radon concentrations where this is possible (the population strategy). Given that 10–20% of the annual cases of lung cancer (300–600 cases) are not attributable to smoking (17), those 12% of the cases that are attributable to radon among never-smokers can be assumed to number fewer than 100.

For smokers who do not want to or are unable to quit, a reduction of radon concentration in their homes may be the most important measure to reduce the risk of lung cancer. Doctors should be aware of this aspect when providing advice on risk reduction.

Received 10.2.2016, first revision submitted 19.8.2016, accepted 5.4.2017.

CHRISTINA SØYLAND HASSFJELL

(born 1969), doctor and dr.scient. (PhD, radiation physics and radiobiology). During this work she was senior adviser associated with the Centre for Environmental Radioactivity (CERAD). The author has completed the ICMJE form and declares no conflicts of interest.

TOM KRISTIAN GRIMSRUD

(born 1955), MD, PhD (cancer epidemiology) and specialist in occupational medicine, with experience from environmentally and occupationally related causal research, senior consultant and researcher.

The author has completed the ICMJE form and declares no conflicts of interest.

WILLIAM J.F. STANDRING

(born 1970), dr. scient. (PhD in environmental chemistry) and senior researcher.

The author has completed the ICMJE form and declares no conflicts of interest.

STEINAR TRETLI

(born 1949), dr.philos. (cancer epidemiology), cand.real. (mathematical statistics) and senior researcher.

The author has completed the ICMJE form and declares no conflicts of interest.

REFERENCES

- 1 Cancer Registry of Norway. Cancer in Norway 2015 - cancer incidence, mortality, survival and prevalence in Norway. Oslo: Kreftregisteret, 2016.
- 2 Zeeb H, Shannoun F. red. WHO handbook on indoor radon: a public health perspective. Genève: World Health Organization, 2009.
- 3 Darby S, Hill D, Auvinen A et al. Radon in homes and risk of lung cancer: collaborative analysis of individual data from 13 European case-control studies. BMJ 2005; 330: 223.
- 4 IARC, International Agency for Research on Cancer. A review of human carcinogens. Part D. Radiation: internalized α-particle emitting radionuclids. IARC monographs on the evaluation of carcinogenic risks to humans. Volume 100 D: 241–83. Lyon: IARC, 2012
- 5 Darby S, Hill D, Deo H et al. Residential radon and lung cancer-detailed results of a collaborative analysis of individual data on 7148 persons with lung cancer and 14,208 persons without lung cancer from 13 epidemiologic studies in Europe. Scand J Work Environ Health 2006; 32:1-83.
- 6 Krewski D, Lubin JH, Zielinski JM et al. Residential

- radon and risk of lung cancer: a combined analysis of 7 North American case-control studies. Epidemiology 2005; 16:137-45.
- 7 Krewski D, Lubin JH, Zielinski JM et al. A combined analysis of North American case-control studies of residential radon and lung cancer. J Toxicol Environ Health A 2006; 69: 533–97.
- 8 Lubin JH, Wang ZY, Boice JD et al. Risk of lung cancer and residential radon in China: pooled results of two studies. Int J Cancer 2004; 109: 132-7.
- 9 Committee on Health Risks of Exposure to Radon. Health effects of exposure to radon (BEIR VI). Washington D.C.: National Academy Press, 1999.
- 10 Statens strålevern. Kartlegging av radon i 114 kommuner. Kort presentasjon av resultater. Strålevernrapport 2001:6. Østerås: Statens strålevern, 2001.
- 11 Statens strålevern. Måling av radon i inneluft og undersøkelser av byggegrunn. Strålevernhefte 3, 1998. Østerås: Statens strålevern, 1998.
- 12 Fleten C. red. Miljørettet helsevern; kjemiske, fysiske og biologiske miljøforholds betydning for helse i vårt land og fordelingen av disse.

- FHI-rapport 2009:7. Oslo: Folkehelseinstituttet, 2009. https://www.fhi.no/publ/eldre/rapport-20097-miljorettet-helsevern/ (5.4.2017).
- 13 AGIR Advisory Group on Ionising Radiation. Radon and public health: report of the independent Advisory Group on Ionising Radiation. Chilton: Health Protection Agency, 2009.
- 14 Magnus P, Bakketeig LS. Epidemiologi. 3. utg. Oslo: Gyldendal Akademisk, 2003.
- 15 Axelsson G, Andersson EM, Barregard L. Lung cancer risk from radon exposure in dwellings in Sweden: how many cases can be prevented if radon levels are lowered? Cancer Causes Control 2015; 26: 541-7.
- 16 TEK 10: Forskrift om tekniske krav til byggverk (Byggteknisk forskrift). Oslo: Kommunal- og moderniseringsdepartementet, 2010. https://lovdata.no/dokument/SF/forskrift/ 2010-03-26-489 (5.4.2017).
- 17 Nasjonalt handlingsprogram med retningslinjer for diagnostikk, behandling og oppfølging av lungekreft, mesoteliom og thymom. Oslo: Helsedirektoratet. 2015.