Meta-analysis of residential exposure to radon gas and lung cancer

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Objectives To investigate the relation between residential exposure to radon and lung cancer.
Methods A literature search was performed using Medline and other sources. The quality of studies was assessed. Adjusted odds ratios with 95% confidence intervals (CI) for the risk of lung cancer among categories of levels of exposure to radon were extracted. For each study, a weighted log–linear regression analysis of the adjusted odds ratios was performed according to radon concentration. The random effect model was used to combine values from single studies. Separate meta-analyses were performed on results from studies grouped with similar characteristics or with quality scores above or equal to the median.
Findings Seventeen case–control studies were included in the meta-analysis. Quality scoring for individual studies ranged from 0.45 to 0.77 (median, 0.64). Meta-analysis based on exposure at 150 Bq/m^3 gave a pooled odds ratio estimate of 1.24 (95% CI, 1.11–1.38), which indicated a potential effect of residential exposure to radon on the risk of lung cancer. Pooled estimates of fitted odds ratios at several levels of radon exposure were all significantly different from unity — ranging from 1.07 at 50 Bq/m^3 to 1.43 at 250 Bq/m^3. No remarkable differences from the baseline analysis were found for odds ratios from sensitivity analyses of studies in which >75% of eligible cases were recruited (1.12, 1.00–1.25) and studies that included only women (1.29, 1.04–1.60).
Conclusion Although no definitive conclusions may be drawn, our results suggest a dose–response relation between residential exposure to radon and the risk of lung cancer. They support the need to develop strategies to reduce human exposure to radon.

Keywords Radon/adverse effects; Lung neoplasms/chemically induced; Environmental exposure; Residence characteristics; Households; Case-control studies; Cohort studies; Meta-analysis (*source: MeSH, NLM*).

Mots clés Radon/effets indésirables; Tumeur poumon/induit chimiquement; Exposition environnement; Caractéristiques habitat; Ménages; Etude cas-témoins; Etude cohorte; Méta-analyse (*source: MeSH, INSERM*).

Palabras clave Radón/efectos adversos; Neoplasmas pulmonares/inducido químicamente; Exposición a riesgos ambientales; Distribución espacial; Hogares; Estudios de casos y controles; Estudios de cohortes; Meta-análisis (*fuente: DeCS, BIREME*).

الـكلمات المفتاحية: الرادون، التأثيرات الضائرة للرادون، أورام الرئة، أورام الرئة المحرضة كيميائياً، التعرض البيئي، خصائص المسكن، السكان، دراسات الحالات والشواهد، دراسات الأتراب، تحليل تلوي. (**المصدر: قائمة رؤوس الموضوعات الطبية– المكتب الإقليمي لشرق المتوسط**).

Bulletin of the World Health Organization 2003;81:732-738

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يمكن الاطلاع على الملخص بالعربية في صفحة ٧٣٧

Introduction

The role of radon as a risk factor for lung cancer in occupational settings, such as underground mining, has been documented in several studies (*1–4*), whereas the risk associated with residential exposure to radon remains controversial. Radon-222 — a ubiquitous radioactive gas — is present in the earth's crust and emerges from soils and rocks. It represents, with its progeny, one of the main sources of exposure to radioactivity in humans, as it emits alpha particles that may damage lung tissues after inhalation. Outdoor concentrations of radon generally are low; a cause for concern is the concentrations inside buildings, where radon can penetrate from subsoil, may be included in building materials, and may be found in water. Indoor concentrations of radon may vary depending on the concentration of radon in the soil; the permeability of the ground; and the construction, building materials, and ventilation of the house.

Attempts to extrapolate data from occupational studies to estimate the risk associated with residential exposure to radon have been criticized because of possible differences in levels of exposure between underground miners and people in the indoor environment and because of several other factors — e.g. possible effects of other concurrent lung carcinogens in miners, differences in particle size distribution, and differences in breathing rates (*5–7*). Findings of large-scale observational studies (particularly case–control studies) of the effects of residential exposure to radon in different countries have produced conflicting results — some confirm the data found in miners (*8–13*), while others could not find any association between exposure to radon and lung cancer (*14–16*). A trend towards positive results has been noted in more recent studies, however; this has been attributed to the use of enhanced radon dosimetry (*10*).

Meta-analysis is a quantitative approach that has been used successfully, particularly to pool results of randomized clinical trials and observational studies to draw conclusions that were not so clear from individual studies. Recently, this approach has been applied in three meta-analyses to examine the relation between residential radon exposure and lung cancer (*17–19*). We used a meta-analysis to update these results and further our understanding of the relation between residential exposure to radon and lung cancer.

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Ref. No. **02-000653**

Materials and methods

Identification of relevant studies

We identified references about the association between residential radon exposure and lung cancer in the general population by using Medline to search the medical literature published in English from 1966 to December 2002. We supplemented this search by reviewing the reference lists of the identified papers to look for studies the computer search might have missed. Inclusion criteria for studies are given in Box 1.

Quality scoring

To assess the quality of the research included in a meta-analysis, each article was read and scored for quality by two independent readers, who were blinded to authors, institutions, country, and journal, with a system that incorporated elements of methods developed by Chalmers et al. (*20*) and Angelillo & Villari (*21*). The readers discussed their evaluation, and any disagreements were resolved through discussion and rereading. The overall quality score of each study was calculated from four subscores for study design (score ranging from 0 to 8 from worst to best), adjustment of confounding variables (0–9), exposure assessment (0–9), and data analysis (0–5). Each subscore was calculated as the percentage of applicable quality criteria that were met in each study, so for each subscore, a study could have a total from 0% (no quality criteria met) to 100% (all quality criteria met). The criteria used are listed with the results in Table 1. The cumulative quality score was a weighted average of the four percentages.

Data extraction

Data on time-weighted mean radon concentrations and cumulative exposure to radon were extracted from the studies. The studies used a number of different categories to indicate the level of indoor exposure, and each paper identified different cut-off levels for radon exposure. All studies stratified by level of exposure to evaluate dose–response relations and performed some stratified or multivariate analysis to adjust for a number of confounders. For the published results of each of the selected studies, we extracted adjusted odds ratios with 95% confidence intervals for the risk of lung cancer among categories of exposure to residential radon concentration measured in becquerels per cubic metre (Bq/m^3). Two readers extracted data independently and then met to resolve any differences and arrive at a consensus.

Meta-analysis

For each study, a weighted log–linear regression analysis of the adjusted odds ratios was performed according to the mean, median, or midpoint concentration of radon; in the presence of open-ended categories, values of radon concentrations proportional to those of the other categories were chosen. Weights were calculated according to Greenland, and Berlin et al. (*22, 23*). Coefficients and 95% confidence intervals were calculated from the model according to several levels of radon concentration. The random effect model described by DerSimonian & Laird was used to combine the values from the single studies (*24*). This model calculates a weighted average of the odds ratio by incorporating within-study and between-study variations. Compared with the fixed effect model of Mantel & Haenszel (*25*), DerSimonian & Laird's model generally gives a more conservative estimate of the odds ratio, with a wider confidence interval if heterogeneity is present (*24*). Data were analysed with Stata software (version 6.0).

> Box 1. **Inclusion criteria for studies to be included in meta-analysis**
>
> - Primary study (not reanalysis or review)
> - Case–control or cohort design
> - Examined residential based exposures to radon with a long-term alpha-track detector to give time-weighted mean concentrations and/or cumulative exposures
> - Examined lung cancer
> - Reported enough data to estimate the odds ratio and its variance
> - Published in English
> - Published by December 2002

Sensitivity analyses

As heterogeneity of studies may be related to several factors (such as study design, characteristics of participants, modes of recruitment, adjustment for confounding, and assessment of exposure), we performed separate meta-analyses by grouping studies that had similar characteristics — such as those that recruited >75% of eligible cases, adjusted for socioeconomic status, restricted recruitment to women, took radon measurements in ≥70% of all houses lived in during the previous 20–30 years, and adjusted for mean time spent at home. Finally, we performed a sensitivity analysis to determine the potential impact of the quality of studies on the results, by pooling only studies with scores greater than or equal to the median.

Results

Literature search

Of the original 89 studies identified, 67 were excluded because they were not case–control or cohort studies that examined the association between exposure to residential radon and lung cancer. Of the remaining 22 studies, all of which were case–control studies, three were reanalyses and two did not allow extraction of data for meta-analysis and therefore were excluded. Overall, we included 17 case–control studies in the meta-analysis (Table 2, web version only, available at: http://www.who.int/bulletin) (*8–16, 26–33*). Of the studies that considered time-weighted mean measurements, one classified exposure in three categories, eight in four categories, five in five categories, and two in six categories; all those that considered cumulative measurements separated exposure into four categories. Numbers of cases and controls enrolled ranged from 28 to 1449 and from 35 to 3185, respectively. Baseline level of exposure ranged from ≤24 to <100 Bq/m^3 in studies that used time-weighted means and 0–463 to 0–1800 Bq/m^3 for cumulative exposure. Adjusted odds ratios in single levels of exposures were significantly higher compared with the reference category in eight single-level comparisons that used time-weighted measurements and in three that used cumulative measurements.

Quality assessment

Table 1 shows the results of the quality scoring procedure. Quality scoring for individual studies ranged from 0.45 to 0.77 (median, 0.64). The largest concern with respect to study design was with response rates, which were >75% in only 35.3% of cases and 23.5% of controls. Other criteria, such as mode of selection of cases and controls, identification of cases without knowledge of exposure status, no known association between control status and exposure, and validation of disease

Table 1. **Items used to quality score studies of the association between exposure to indoor radon and lung cancer**

Quality scoring item	Studies complying[a]
Study design	
Cases either randomly selected or selected to include all cases in a specific population	16 (94.1)[b]
Cases identified without knowledge of exposure status	17 (100)
Response rate for identified cases >75%	6 (35.3)
Control drawn randomly from the same population of cases	16 (94.1)
No known association between control status and exposure	16 (94.1)
Response rate for identified controls >75%	4 (23.5)
Specific disease criteria given	13 (76.5)
Disease validated by histology or other gold standard	15 (88.2)
Adjustment or matching for confounders	
Age	17 (100)
Smoking	17 (100)
Duration	13 (76.5)
Intensity	15 (88.2)
Sex	17 (100)
Occupation	10 (58.8)
Socioeconomic status or education	9 (52.9)
Diet	4 (23.5)
Ambient air quality (e.g. traffic density)	4 (23.5)
Exposure assessment	
Exposure assessment made blindly in respect to the case–control status of participants	0 (0)
Exposure evaluations made in relation to the time of diagnosis	16 (94.1)
Radon measurements lasting more than one year	14 (82.3)
Indoor radon measured in more than one location	11 (64.7)
Evaluation of historical indoor radon levels	9 (52.9)
Residence in the current home for 20 consecutive years or more	3 (17.6)
Radon measurement in ≥70% of houses lived in during the previous 20–30 years	6 (35.3)
Outdoor radon concentrations	1 (5.9)
Radon measurement adjusted for mean time spent at home	6 (35.3)
Data analysis	
Demographic data listed	14 (82.3)
Statistical analysis of demographic data	5 (29.4)
Power calculations performed	0 (0)
Precise P-values and/or confidence interval given	17 (100)
Test statistic specified	17 (100)

[a] If compliance is not specifically indicated in the text, non-compliance is assumed.
[b] Values in parentheses are percentages.

diagnosis by histology or other gold standards were satisfied by 88.2–100% of the studies. In most studies, exposure assessment was performed with a sufficient time-window before diagnosis (⩾20 years) (94.1%), was performed for ⩾1 year (82.3%), and involved more than one location in the house (64.7%). Few studies took into account the mean time spent at home (35.3%), considered only participants who had lived in the current home for ⩾20 consecutive years (17.6%), or had taken radon measurements in ⩾70% of the houses in which participants had lived in the previous 20–30 years (35.3%). Only one study had measured outdoor radon concentrations.

Potential confounders generally were not adjusted for, with the exception of age, sex, and smoking, which were adjusted for in all studies. Not all studies adjusted for the quantitative effect of smoking: 76.5% included some indicator of duration (such as age at starting smoking) and 88.2% some indicator of intensity of smoking (such as cigarette pack-years). Statistical analysis included multivariate analysis with adjustment for confounders; all studies listed *P*-values and confidence intervals. Lower scores in data analyses were related to failure to list and perform statistical analyses of demographic data.

Meta-analysis

Table 3 shows the adjusted odds ratio estimates at an exposure level to radon of 150 Bq/m^3 from each study and the overall result of each single meta-analysis for several levels of exposure to radon. Of the 17 estimates of the single studies derived from the log–linear model, 10 were significantly greater than 1.00, which suggested an association of indoor exposure to radon with lung cancer. In two cases, the 95% confidence intervals were below unity; in the remaining five cases, the 95% confidence intervals included one, which suggested no significant effect. The meta-analysis based on exposure at 150 Bq/m^3 in the time-weighted mean measurements gave a pooled odds ratio estimate of 1.24 (95% confidence interval, 1.11–1.38), which indicated a potential effect of residential radon exposure on lung cancer.

Table 3. **Summary results of meta-analyses relating indoor radon and lung cancer**

Study	Adjusted odds ratio[a] at 150 Bq/m³
Blot et al. (1990)	0.95 (0.93–0.97)[b]
Shoenberg et al. (1992)	3.06 (2.46–3.79)
Pershagen et al. (1992)	1.38 (1.37–1.40)
Alavanja et al. (1994)	1.07 (0.99–1.16)
Létourneau et al. (1994)	0.98 (0.93–1.04)
Pershagen et al. (1994)	1.18 (1.13–1.23)
Auvinen et al. (1996)	1.02 (0.99–1.04)
Ruosteenoja et al. (1996)	1.47 (1.05–2.04)
Darby et al. (1998)	1.16 (1.06–1.27)
Alavanja et al. (1999)	0.81 (0.72–0.90)
Field et al. (2000)	1.49 (1.35–1.65)
Sobue et al. (2000)	1.32 (0.63–2.73)
Kreienbrock et al. (2001)	1.03 (0.93–1.14)
Lagarde et al. (2001)	1.43 (1.19–1.72)
Pisa et al. (2001)	1.92 (1.06–3.50)
Wang et al. (2002)	1.19 (1.14–1.25)
Barros-Dios et al. (2002)	2.69 (1.34–5.39)
Overall	1.24 (1.11–1.38)
Overall results of meta-analysis by exposure level (Bq/m³)	
50	1.07 (1.04–1.11)
100	1.15 (1.07–1.24)
200	1.33 (1.15–1.54)
250	1.43 (1.19–1.72)

[a] Estimates of single studies fitted from the weighted log–linear regression models.

[b] Figures in parentheses are 95% confidence intervals.

Pooled estimates of fitted odds ratios at several levels of radon exposure were all significantly different from unity — ranging from 1.07 at 50 Bq/m³ to 1.43 at 250 Bq/m³. Homogeneity among studies was rejected, however, as the test for heterogeneity showed Q = 1220.9 (16 degrees of freedom) and P<0.001.

Table 4 gives the results of all sensitivity analyses. In the baseline analysis, we included the adjusted estimates of each study, regardless of the number and types of confounders chosen by each study. In the meta-analysis that looked at only studies that adjusted for socioeconomic status, no remarkable difference from the baseline analysis was found in estimates of the odds ratio (1.22, 1.07–1.38); this was also the case for the analyses that included only studies that measured exposures in >70% of residences occupied in the previous 20–30 years (1.22, 1.10–1.35) and studies that adjusted for time spent at home (1.23, 1.03–1.47). Lower estimates of odds ratios than in the baseline analysis were found in the meta-analysis that included only studies in which >75% of eligible cases were recruited (1.12, 1.00–1.25), whereas higher estimates emerged in the analyses that included studies restricted to women (1.29, 1.04–1.60) and high quality studies (1.27, 1.15–1.41). In all sensitivity analyses, however, the test of homogeneity of the estimates was rejected (P<0.001).

Discussion

Our meta-analysis suggests a significantly increased risk of lung cancer in people exposed to radon gas in their homes. This association seems to be dose related, and an increase of 24% in the risk of lung cancer was found at a time-weighted mean exposure of 150 Bq/m³. Meta-analyses previously conducted with different methods found significantly increased risks of lung cancer of 6–35% in participants exposed to residential radon at levels of 100–150 Bq/m³ (*17–19*). These results show a consistent pattern of risk related to indoor exposure to radon, although the magnitude of the risk seems to be low. Our findings thus strongly support the need for information about indoor radon concentrations as a prerequisite to developing strategies for action in different geographical locations.

Heterogeneity of studies, potential for misclassification of exposure, and role of confounding (particularly when, as in our case, expected risks are low) may determine problems in the interpretation of results of meta-analyses. Although results are always to be interpreted cautiously, however, sensitivity analyses that take into account these issues may help test the robustness of results. We performed sensitivity analyses with adjustments for socioeconomic status, assessment of exposure in past residences, time spent at home, completeness of recruitment of studies, and quality of studies. The quality of the studies was evaluated on the basis of study design, exposure assessment, data analysis, and adjustment for confounding factors. Although we did not use quality scores to choose studies to include in our meta-analysis (*34*), pooling of high-quality studies resulted in a similar, or at least more strong, association with respect to the baseline meta-analysis. It should be noted, however, that sometimes the amount of information that is included in a published work depends on the journal, so the quality score

Table 4. **Sensitivity of summary results of meta-analyses relating indoor radon and lung cancer according to several sources of potential heterogeneity**

Variable	Studies	Summary odds ratio at 150 Bq/m³
Baseline analysis	17	1.24 (1.11–1.38)[a]
Adjustment for socioeconomic status	9	1.22 (1.07–1.38)
Response rate for identified cases >75%	6	1.12 (1.00–1.25)
More than 70% residence measured	6	1.22 (1.10–1.35)
Radon measurement adjusted for mean time spent at home	6	1.23 (1.03–1.47)
Women only	6	1.29 (1.04–1.60)
High-quality studies	9	1.27 (1.15–1.41)

[a] Figures in parentheses are 95% confidence intervals.

may correlate with publication criteria. Most studies were similar in design, and detection of exposure and quality scores were not substantially different.

All case–control studies included in the meta-analysis performed some adjustment for confounders, and this is a strength of our results. Little is known about the factors associated with lung cancer and exposure to radon, however, so the effect of some potential confounders on results of single studies and, therefore, on our meta-analysis cannot be ruled out. A substantial number of studies have looked at factors associated with residential radon concentration — such as age of house, ventilation, and number of floors — but few could be classified as important confounders in the association with lung cancer, particularly after aspects related to socioeconomic status, which were included in our sensitivity analysis, are accounted for.

Pooling of studies restricted to women gave a higher estimated odds ratio. This is interesting, as it is well known that women have a lower incidence of lung cancer because of lower exposure to established risk factors, such as smoking and some occupational carcinogens. Women thus may represent a population less prone to confounders when the effect of radon on risk of lung cancer is studied. Our results cannot exclude the possibility that any inability to completely adjust for smoking or some other confounders is responsible for the increased risk detected. Smoking has also been suggested as an effect modifier (*35*), however, in which case the effect of radon should be assessed separately in smokers and non-smokers.

Repeated reports have stated that the retrospective assessment of exposure in case–control studies that investigate environmental risk factors is challenging. This relates to residential exposure to radon that has been reported to be biologically important in the 15–20 years before development of lung cancer, and the inability to detect an association in certain studies might have been due to poor retrospective assessment (*11*). We did not find, however, any relevant difference from the overall analysis in estimates that included only studies that measured radon in >70% of previous houses or adjusted for time spent at home. The need for more reliable and advanced methods has been advocated (*36*), and new methods — such as measurements from glass items present for many years in the houses the participants had lived in — have been used recently and showed an increased risk that was not detected by conventional methods (*10*).

A very cautious approach to the interpretation of our result is related to heterogeneity that we were not able to eliminate by pooling studies that were similar to each other, but none of the variables tested significantly improved homogeneity. Similar results were revealed by Lubin & Boice, who controlled for many similarities and differences among studies in their meta-analysis but were not able to eliminate heterogeneity (*17*).

Conclusion

Although no definitive conclusions can be drawn on the role of radon residential exposure on the risk of lung cancer, our results suggest the existence of a dose–response relation. They reaffirm the usefulness of meta-analyses in the identification of low risks that may elude single studies and support the need for wider and more detailed qualitative and quantitative recognition of the risks of residential exposure to radon and the development of strategies aimed at reduction of human exposure. ■

Conflicts of interest: none declared.

Résumé

Méta-analyse sur l'exposition au radon dans les habitations et le cancer pulmonaire

Objectif Etudier le lien entre l'exposition au radon dans les habitations et le cancer pulmonaire.

Méthodes Nous avons effectué une recherche dans la littérature à l'aide de Medline et d'autres sources et évalué la qualité des études. Nous avons extrait les odds ratios avec un intervalle de confiance (IC) à 95 % pour le risque de cancer pulmonaire aux différents niveaux d'exposition au radon. Pour chaque étude, nous avons procédé à une analyse des odds ratios par régression pondérée selon un modèle log-linéaire en fonction de la concentration en radon. Nous avons utilisé le modèle à effets aléatoires pour associer les valeurs résultant des études prises séparément. Nous avons réalisé d'autres méta-analyses des résultats obtenus à partir d'études regroupées en raison de leurs caractéristiques similaires ou auxquelles on a attribué une note de qualité supérieure ou égale à la médiane.

Résultats La méta-analyse a couvert 17 études cas-témoins. Les notes de qualité pour chaque étude se sont situées entre 0,45 et 0,77 (médiane de 0,64). La méta-analyse, basée sur une exposition à 150 Bq/m^3, a donné une estimation de l'odd ratio global à 1,24 (IC 95 % : 1,11 – 1,38), ce qui indique un effet potentiel de l'exposition au radon dans les habitations sur le risque de cancer pulmonaire. Les estimations communes des odds ratios ajustés à plusieurs niveaux d'exposition au radon ont toutes abouti à des différences significatives par rapport à l'unité, de 1,07 pour 50 Bq/m^3 à 1,43 pour 250 Bq/m^3. On n'a pas constaté de différences marquantes par rapport aux analyses de référence pour les odds ratios obtenus à partir des analyses de sensibilité sur les études ayant recruté plus de 75 % des cas répondant aux critères d'inclusion (1,12, 1,00 – 1,25) et sur les études portant seulement sur les femmes (1,29, 1,04 – 1,60).

Conclusion Bien qu'il soit impossible de tirer des conclusions définitives, nos résultats donnent à penser qu'il existe une relation dose-réponse entre l'exposition au radon dans les habitations et le risque de cancer pulmonaire. Ils confortent la nécessité d'élaborer des stratégies pour réduire l'exposition de l'être humain au radon.

Resumen

Metanálisis de la exposición residencial al gas radón y el cáncer de pulmón

Objetivo Investigar la relación entre la exposición residencial al radón y el cáncer de pulmón.

Métodos Se realizó una búsqueda de bibliografía a partir de MEDLINE y otras fuentes, evaluándose la calidad de los estudios. Se extrajeron las razones de posibilidades ajustadas con intervalos de confianza (IC) del 95% para el riesgo de cáncer de pulmón a distintos niveles de exposición al radón. Para cada estudio, se efectuó un análisis de regresión log-lineal ponderada de las razones de posibilidades ajustadas en función de la concentración de radón. Se usó el modelo de efectos aleatorios para combinar los valores de estudios individuales, y se realizaron metanálisis independientes de los resultados de grupos de estudios de características similares o con puntuaciones de la calidad superiores o iguales a la mediana.

Resultados Se incluyeron en el metanálisis 17 estudios de casos y controles. Las puntuaciones de la calidad de los estudios se situaron entre 0,45 y 0,77 (mediana = 0,64). El metanálisis basado en la exposición a 150 Bq/m^3 arrojó una estimación de la razón de posibilidades combinada de 1,24 (IC95% = 1,11–1,38), indicativa de un posible efecto de la exposición residencial al radón en el riesgo de cáncer de pulmón. Las estimaciones combinadas de las razones de posibilidades ajustadas a varios niveles de exposición al radón fueron todas significativamente diferentes de la unidad, entre 1,07 a 50 Bq/m^3 y 1,43 a 250 Bq/m^3. No se hallaron diferencias marcadas respecto a los análisis basales para las razones de posibilidades de los análisis de sensibilidad de los estudios en que se reclutó a más del 75% de los casos elegibles (1,12, 1,00–1,25) y los estudios que incluyeron sólo mujeres (1,29, 1,04–1,60).

Conclusión Aunque no es posible extraer conclusiones definitivas, nuestros resultados sugieren una relación dosis–respuesta entre la exposición residencial al radón y el riesgo de cáncer de pulmón, y corroboran la necesidad de formular estrategias para reducir la exposición humana a ese elemento.

ملخص

التحليل التلوي للتعرض المترلي لغاز الرادون وسرطان الرئة

الهدف: البحث عن العلاقة بين التعرض.المترلي لغاز الرادون وسرطان الرئة.

الطريقة: أجري بحث في المنشورات الطبية عبر خط استرجاع النشريات الطبية "ميدلاين" ومصادر أخرى، وتم تقييم جودة الدراسات، وتم استخلاص نسب الأرجحية المصححة بفواصل ثقة ٩٥٪ بالنسبة لأخطار سرطان الرئة بين الفئات المقسمة وفقاً لمستوى التعرض للرادون. وقد أجري في كل دراسة علىٍ حدة تحليل تحوف للوغارتيم الخطي الموزون لكل من نسب الأرجحية وفقاً لتركيز الرادون. وقد تم استخدام نموذج تأثير عشوائي لضم القيم المستخلصة من دراسات فردية، ثم أجري تحليل تلوي منفصل على النتائج المستخلصة من الدراسات المجمعة في مجموعات متشابهة الخواص مع أو بدون أحراز للجودة تعادل أو تزيد عن الوسطي.

الموجوًدات: أدخلت ١٧ دراسة للحالات والشواهد في التحليل التلوي. وتراوحت أحراز الجودة لكل دراسة على حدة بين ٠,٤٥ و ٠,٧٧ (الوسطي ٠,٤٦). وقد بني التحليل التلوي على أن التعرض لمقدار ١٥٠ بيكريل لكل متر مكعب سيؤدي لنسب الأرجحية مجتمعة تقدر بـ ١,٢٤(بفاصلة ثقة ٩٥٪ وتتراوح بين ١,١١ و ١,٣٨)، وهذا يشير إلى احتمال تأثير التعرض المترلي للرادون في اختطار الإصابة بسرطان الرئة. وقد كانت التقديرات المجمَّعة لنسب الرجحان المناسبة لمستويات مختلفة من التعرض للرادون مختلفة اختلافاً هاماً عن بعضها ويتراوح الاختلاف بين ١,٠٧ في مستوى التعرض لمقدار ٥٠ بيكريل لكل متر مكعب و ١,٤٣ في في مستوى التعرض لمقدار ٢٥٠ لكل متر مكعب. و لم تلاحظ اختلافات جوهرية في التحليل الأساسي لنسبة الأرجحية عن تحاليل الحساسية للدراسات التي كان فيها ما يزيد عن ٧٥٪ من الحالات قد استجلبت (وكانت فاصلة الثقة تتراوح بي ١,١٢ و ١,٠٠ إلى ١,٢٥ وللدراسات التي اقتصرت على النساء فقط (كانت فاصلة الثقة تتراوح بين ١,٢٩ و ١,٠٤ إلى ١,٦٠).

النتيجة: رغم أننا لم نستطع التوصل إلى نتيجة حاسمة فإن حصيلة ما توصلنا إليه تشير إلى وجود علاقة الجرعة -الاستجابة بين التعرض المترلي للرادون وبين اختطار الإصابة بسرطان الرئة. وهذا ما يدعم الحاجة لإعداد استراتيجيات لخفض تعرض الناس للرادون.

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Table 2. **Studies included in meta-analysis of studies of the relation between indoor exposure to radon and lung cancer**

Study	Country	Age range of participants (years)	Group size (case/control)	Adjustment and matching	Level of exposure (Bq/m³)			
					Time-weighted mean		Cumulative exposure	
					Level	Adjusted odds ratio	Level	Adjusted odds ratio
Blot et al. (*14*)	China	30–69[a]	308/356	Age, sex, smoking, socioeconomic status, and ambient air quality	<74 74–147 148–295 ⩾296	1.00 0.9 (0.6–1.3)[b] 0.9 (0.5–1.4) 0.7 (0.4–1.3)		
Schoenberg et al. (*26*)	USA	All ages[a]	480/442	Age, sex, smoking, socioeconomic status, occupation, and diet	<37 37–73 74–147 148–418	1.00 1.2 (0.83–1.7) 1.1 (0.55–2.3) 8.7 (1.3–57.8)	<463 463–924 925–1849 1850–2868	1.00 1.3 (0.88–1.9) 0.91 (0.41–2.00) 8.0 (1.2–55.1)
Pershagen et al. (*27*)	Sweden	All ages[a]	210/209	Age, sex, and smoking	<75 75–110 111–150 ⩾151	1.00 1.2 (0.7–2.1) 1.3 (0.7–2.3) 1.7 (1.0–2.4)	⩽1250 1251–2500 2501–5000 ⩾5001	1.00 1.4 (0.8–2.6) 1.7 (1.0–3.1) 2.3 (1.1–4.5)
Alavanja et al. (*15*)	USA	All ages[a]	538/1183	Age, sex, smoking, socioeconomic status, and diet	<30 30–43 44–63 64–91 >91	1.00 1.01 (0.7–1.4) 0.84 (0.6–1.3) 0.9 (0.6–1.3) 1.2 (0.9–1.7)		
Létourneau et al. (*16*)	Canada	35–80	738/738	Age, sex, smoking, socioeconomic status, and occupation			0–1800 1801–3600 3601–7200 ⩾7201	1.00 0.97 (0.63–1.48) 0.84 (0.51–1.39) 1.00 (0.69–1.46)
Pershagen et al. (*28*)	Sweden	35–74	1360/2847	Age, sex, smoking, occupation, and ambient air quality	⩽50 51–80 81–140 141–400 >400	1.00 1.1 (0.9–1.3) 1.0 (0.8–1.3) 1.3 (1.1–1.6) 1.8 (1.1–2.9)		
Auvinen et al. (*8*)	Finland	All ages	1055/1544	Age, sex, smoking, and occupation	⩽49 50–99 100–199 200–399 400–1277	1.00 1.03 (0.84–1.26) 1.00 (0.78–1.29) 0.91 (0.61–1.35) 1.15 (0.69–1.93)		
Ruosteenoja et al. (*29*)	Finland	0–64[c]	164/331	Age, sex, smoking, and ambient air quality	⩽95 96–186 ⩾187	1.00 1.8 (0.9–3.5) 1.5 (0.8–2.9)		
Darby et al. (*9*)	UK	<75	982/3185	Age, sex, smoking, socioeconomic status, occupation, and diet	<25 25–49 50–99 100–199 200–399 ⩾400	1.00 1.06 (0.88–1.29) 1.13 (0.89–1.44) 1.29 (0.79–2.12) 0.94 (0.68–1.29) 1.79 (0.74–4.33)		
Alavanja et al. (*10*)	USA	30–84[a]	247/299	Age, sex, smoking, socioeconomic status, and diet	<37 37–73 74–147 ⩾148	1.00 0.87 (0.6–1.3) 0.91 (0.5–1.5) 0.71 (0.3–1.3)		

(Table 2, cont.)

Study	Country	Age range of participants (years)	Group size (case/ control)	Adjustment and matching	Level of exposure (Bq/m³)			
					Time-weighted mean		Cumulative exposure	
					Level	Adjusted odds ratio	Level	Adjusted odds ratio
Field et al. (*11*)	USA	40–84[a]	413/614	Age, sex, smoking, and socioeconomic status	≤57 58–114 115–170 171–228 >228	1.00 1.34 (0.81–2.22) 1.73 (0.99–3.04) 1.62 (0.88–2.99) 1.79 (0.99–3.26)		
Sobue et al. (*30*)	Japan	≥65	28/35	Age, sex, smoking, and occupation	≤24 25–49 50–99 ≥100	1.00 1.13 (0.29–4.4) 1.23 (0.16–9.39) 0.25 (0.03–2.33)		
Kreienbrock et al. (*12*)	Germany	≤75	1449/2297	Age, sex, smoking, and occupation	<50 50–80 81–140 >140	1.00 0.98 (0.81–1.2) 1.09 (0.8–1.48) 0.99 (0.61–1.63)		
Lagarde et al. (*13*)	Sweden	>29	86/178	Age, sex, smoking, socioeconomic status, occupation, and ambient air quality	<50 50–80 81–140 >140	1.00 1.03 (0.67–1.57) 1.14 (0.72–1.8) 1.65 (0.88–2.7)		
Pisa et al. (*31*)	Italy	All ages	138/291	Age, sex, smoking, and occupation	<40 40–76 77–139 140–199 ≥200	1.00 2.00 (1.00–3.9) 1.8 (0.9–6.2) 2.4 (0.9–6.2) 1.00 (0.3–3.1)		
Wang et al. (*32*)	China	All ages	768/1659	Age, sex, smoking, residence, occupation, and socioeconomic status	<100 100–149 150–199 200–249 250–299 ≥300	1.00 1.00 (0.7–1.5) 1.42 (1.00–2.00) 1.36 (1.00–1.9) 1.28 (0.8–1.9) 1.58 (1.1–2.3)		
Barros-Dios et al. (*33*)	Spain	≥35	163/241	Age, sex, smoking, and family history	0–37 37–55.1 55.2–147.9 ≥148	1.00 2.73 (1.12–5.48) 2.48 (1.29–6.79) 2.96 (1.29–6.79)		

[a] Women only.
[b] Values in parentheses are 95% confidence intervals.
[c] Men only.