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Lung cancer mortality attributable to residential radon exposure in Spain and its regions

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A R T I C L E I N F O

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A B S T R A C T

Lung cancer has the highest cancer mortality rate in developed countries. The principal risk factor for lung cancer is tobacco use, with residential radon being the leading risk factor among never smokers and the second among ever smokers. We sought to estimate mortality attributable to residential radon exposure in Spain and its Autonomous Regions, with correction for dwelling height and differentiation by tobacco use. We applied a prevalence-based method for estimating attributable mortality. For estimations, we considered exposure to radon in the different Autonomous Regions corrected for dwelling height, using the National Statistics Institute Housing Census and prevalence of tobacco use (never smokers, smokers and ex-smokers). The results showed that 3.8% (838 deaths) of lung cancer mortality was attributable to radon exposure of over 100 Bq/m^3, a figure that rises to 6.9% (1,533 deaths) when correction for dwelling height is not performed. By Autonomous Region, the highest population attributable fractions, corrected for dwelling height, were obtained for Galicia, Extremadura, and the Canary Islands, where 7.0, 6.9, and 5.5% of lung cancer mortality was respectively attributable to radon exposure. The greatest part of the attributable mortality occurred in men and among smokers and ex-smokers. Residential radon exposure is a major contributor to lung cancer mortality, though this contribution is highly variable among the different territories, indicating the need for targeted prevention policies. Correction of estimates for dwelling height is fundamental for providing reliable estimates of radon-attributable mortality.

1. Introduction

Lung cancer is currently a major health problem. It is the neoplasm with the second highest incidence in men and also for women in some countries (Ferlay et al., 2012), and accounts for almost 25% of all cancer-related deaths in both sexes, thus reflecting its high lethality (Siegel et al., 2020). Survival at five years of diagnosis stands at around 15–20% (Allemani et al., 2018).

Smoking is the leading risk factor, followed by exposure to residential radon. The WHO indicates that radon exposure is the leading risk factor for lung cancer among never smokers and the second leading risk factor after tobacco use among ever smokers (World Health Organization, 2009). Radon is a gas issuing from the disintegration of radium contained in rocks forming part of the Earth's crust, and is colorless, odorless and tasteless. It was classified as a human carcinogen in 1988 by the International Agency for Research on Cancer (IARC) (Radon, 1988). It releases alpha radiation, and this is also the case of the short half-life radon progeny (polonium 214 and polonium 218), that impacts the cell lining of the lungs when inhaled. Being a gas, it can leak into dwellings and other interior spaces through cracks, fissures or poorly sealed joints, and can reach high concentrations that may increase the risk of lung cancer. Residential radon concentrations essentially depend

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on the characteristics of the building materials used and the radon exhalation rate of rocks in the Earth's crust in which the gas is found, and in the latter case on the uranium content, which is the parent element of the radioactive decay chain series from which radon comes. Within a given country, province, county or even municipality, residential radon concentrations can therefore be enormously variable.

Available studies indicate that radon increases the risk of lung cancer linearly, and that for every increase of 100 Bq/m^3 (100 becquerels per cubic meter) in radon concentration, risk of lung cancer rises by 16% (Darby et al., 2005). Other recent studies have reported that, as compared to subjects exposed to less than 50 Bq/m^3, those exposed to more than 200 Bq/m^3 register an Odds Ratio of 2.06 (95% CI: 1.61–2.64) (Lorenzo-Gonzalez et al., 2020). There is also a higher lung cancer risk for never-smokers. Never smokers exposed to more than 200 Bq/m^3 versus those exposed to less than 100 Bq/m^3 pose an Odds Ratio of 1.73 (95%CI: 1.27–2.35) (Lorenzo-González et al., 2019). A number of studies have reported a sub-multiplicative interaction between radon exposure and tobacco use in lung cancer risk (Lorenzo-Gonzalez et al., 2020; Health Risks of Radon; Barros-Dios et al., 2012).

From an epidemiologic and public-health action stance, it is important to ascertain the lung cancer burden attributable to exposure to radon, while also taking tobacco use into account. This population attributable fraction (PAF) varies importantly among countries in which it has been calculated (Gaskin et al., 2018). With the exception of Galicia, however, there are no studies in Spain that have estimated the lung cancer fraction attributable to residential radon exposure at a population level (Pérez-Ríos et al., 2010).

The residential radon exposure of a country's population is usually estimated on the basis of national radon maps. Most of these maps are plotted with the aim of identifying the geographic areas most exposed to radon, with the result that they follow geographic design criteria and are exclusively based on radon measures taken on the ground floors of buildings or on measures taken of detached single-family dwellings in which radon concentration is estimated as an average of ground- and first-floor concentrations (see European Atlas of Natural Radiation (Cinelli et al., 2019)). This is the case of the Radon Potential Map of Spain (García-Talavera and López, 2019). As against these types of maps, radon maps designed with population criteria (in which all the individuals of a given population have an equal probability of being included in the sampling) directly represent population exposure to radon. This is the case of the map of Italy (Bocchicchio et al., 1999) and the radon map of Galicia (Lorenzo-González et al., 2017).

To our knowledge, none of the available international studies based on maps of the former type envisage correcting radon exposure for dwelling height. Failure to make this correction implies that radon exposure is assigned in accordance with an estimate of concentrations obtained at ground level or on the ground floor. This amounts to an overestimate of radon exposure in homes situated on higher floors, since radon concentrations generally decrease as dwelling height increases. The importance of this misclassification in each country estimates will depend on the percentage of multi-family apartment blocks versus single-family dwellings in the housing sector. In Spain, this correction has almost no effect in the case of rural areas (single-family dwellings) but might well have a discernible impact when estimating attributable mortality (AM) in urban or semiurban areas in which there might be a relevant degree of exposure to radon.

Accordingly, the aim of this study was to estimate lung cancer mortality attributable to radon exposure in Spain and its regions in 2017, applying, for the first time, a correction for population exposure to radon according to dwelling height. We also sought to differentiate AM by sex and tobacco use.

2. Subjects and methods

We applied a method of estimating mortality dependent on the prevalence of radon exposure, based on the calculation of PAFs.

2.1. Data sources

Observed lung cancer mortality. Data were drawn from death statistics broken down by cause of death, sourced from the National Statistics Institute (NSI) (*Instituto Nacional de Estadística*). We used microdata for the year 2017, with number of deaths due to cancer of trachea, lung, and bronchus (ICD-10 codes C33-34) in the population aged 35 years and over, grouped by Autonomous Region (AR), sex, and age group.

Prevalence of exposure to radon. We obtained radon exposure prevalences by AR in three categories (0–100 Bq/m^3, 101–300 Bq/m^3 and >300 Bq/m^3), calculated on the basis of the following cartography: 1) the outlines of 1 km^2 data-dissemination grid cells established by Eurostat, with total population, male, and female indicators, issued by the NSI (NSI, 2011); 2) the Radon Potential Map of Spain (CSN, 2019) (García-Talavera and López, 2019); and 3) the administrative boundaries at a provincial level, generated by the National Geographic Institute. Based on this information, the population distribution per unit of radon potential was obtained for each province. It should be noted that the Radon Potential Map of Spain includes measurements taken exclusively on ground and first floors. Given that the radon concentration measurements in each of these units follow a log-normal distribution, the following probabilities were then estimated for each unit: P(x < 100 Bq/m^3); P(100 Bq/m^3< x < 300 Bq/m^3); and P(x ≥ 300 Bq/m^3). These data were combined with the previous information to obtain radon exposure prevalences by AR. Since radon exposure decreases with dwelling height, we applied a correction for dwelling height. This correction was specific to each AR. To this end, account was taken of the statistics table of buildings intended mainly or exclusively for use as dwellings and the number of properties broken down by the number of floors above ground, available at a provincial level (2011 Population & Housing Census). To establish the corrections due to the effect of dwelling height, the following criteria were considered: 1) dwellings in buildings with one or two floors above ground level were directly assigned the probability distributions shown in the Radon Map of Spain; 2) in the case of dwellings in 3-storey buildings, the above distributions were multiplied by a factor of 0.7; and 3) in the case of dwellings in buildings with 4 or more storeys, the interval <100 Bq/m^3 was assigned to 70% of these, since radon values of over 100 Bq/m^3 are seldom found at this dwelling height, and the probability distributions multiplied by a factor of 0.7 were applied to the remaining 30%. This means that if you have 2,000 dwellings in a third or fourth storeys in a given region (1,000 dwellings per storey), the expected radon distribution is multiplied by 0.7 for those in the third storey. Regarding the fourth storey (and also for higher storeys), 700 dwellings will be assigned to have < 100 Bq/m^3 and for the remaining 300, their expected radon concentration will be multiplied by 0.7. These distributions have been applied using information from a previously published research performed in Spanish dwellings employing real measurements combined with bootstrap estimations (Baixeras et al., 1996).

Populations. We used resident population number at 1 July 2017, by AR, sex, and age group, available on the NSI website.

Prevalences of tobacco use. Prevalences of smokers, ex-smokers, and never smokers in the population aged ≥ 35 years were estimated by AR, sex, and age group, on the basis of combined microdata from three surveys, namely, the 2011 and 2017 National Health Survey of Spain (ENSE-2011 and ENSE-2017) (Ministerio de Sanidad, 2017; Ministerio de Sanidad and Servicios Sociales e Igualdad, 2011), and the 2014 European Health Interview Survey for Spain (*Encuesta Europea de Salud en España/EES2014*) (Ministerio de Sanidad and Consumo y Bienestar Social, 2014).

Lung cancer risks associated with exposure to radon. We obtained Odds Ratios, adjusted for sex, age, and tobacco use, based on a case-control study undertaken in Spain and published in July 2020 (Lorenzo-Gonzalez et al., 2020), which included 3,704 participants (1,842 cases and 1,862 controls) aged 35 years and over.

Lung cancer risks associated with tobacco use. The relative risks were derived from the follow-up of the following five large cohorts: the National Institutes of Health-AARP Diet and Health Study; the American Cancer Society's CPS-II Nutrition Cohort; the Women's Health Initiative; the Nurses' Health Study; and the Health Professionals Follow-Up Study (National Center for Chron, 2014).

2.2. Statistical analysis

Lung cancer AM to radon exposure was estimated for each combination of sex, age group, and AR, as the product of the PAF multiplied by observed mortality (OM): $AM_{s,ij} = PAF_j \times OM_{s,ij}$, where s denotes sex, i the age group (35–54, 55–64, 65–74, 75 years and over), and j the AR. The PAF, which only varies by AR, was calculated considering three radon exposure categories: (0) ≤100 Bq/m^3, (Ferlay et al., 2012) 101–300 Bq/m^3, and (Siegel et al., 2020) >300 Bq/m^3, by means of the expression:

$$PAF_j = \frac{p_{0,j} + p_{1,j}RR_1 + p_{2,j}RR_2 - 1}{p_{0,j} + p_{1,j}RR_1 + p_{2,j}RR_2}$$

where $p_{0,j}, p_{1,j}, p_{2,j}$ are, respectively, the prevalence of exposure to radon in each category in AR(j); RR_k $(k = 1, 2)$ is the relative risk of dying from lung cancer among subjects exposed to radon category k compared with unexposed subjects (category 0), RR_1: 1.33 (1.13–1.57) and RR_2: 1.34 (1.07–1.65), adjusted for sex, age, and tobacco use.

The population attributable fraction is defined as an extension of the formula developed by Levin (Levin, 1953; Walter, 1976) and adapted by Lilienfeld (Lilienfeld et al., 1994).

The number of radon-attributable deaths for each combination of sex, age group, and AR was distributed according to tobacco use, applying the following formulae (subindices s, i, j omitted):

$$\text{Never smokers}: \ AM_{ns} = \frac{AM\ p_{ns}}{p_{ns} + p_{exs}RR_{exs+}p_sRR_s}$$

$$Ex - smokers: AM_{exs} = \frac{AM\ p_{exs}RR_{exs}}{p_{ns} + p_{exs}RR_{exs} + p_sRR_s}$$

$$\text{smokers: } AM_s = \frac{AM\ p_sRR_s}{p_{ns} + p_{exs}RR_{exs} + p_sRR_s}$$

where p_{ns}, p_{exs} and p_s are the prevalences of never smokers, ex-smokers and smokers, respectively, which vary by sex, age group, and AR; RR_{exs} and RR_s are the relative risks of lung cancer mortality in ex-smokers and smokers as compared with never smokers, and vary by sex and age group.

For each AR and sex, we calculated crude lung cancer mortality rates attributable to radon exposure, and rates adjusted for age by the direct method, using the Spanish population resident at 1 July 2017 as standard. In the results, all rates are expressed per 100,000 inhabitants.

We performed a sensitivity analysis using the Darby et al. method to provide an alternative assessment on the estimation of AM. This method is based on radon mean concentration. Information on the methods and results is shown as Supplementary material.

All statistical analysis were carried out with Stata version 14.2 (Stata Corporation, College Station, TX, USA).

3. Results

In 2017, there were 22,121 lung cancer deaths in Spain; of these, 22,063 occurred in the population aged 35 years and over, 17,234 in men and 4,829 in women.

Table 1 shows the population distribution according to radon exposure by AR, as well as the effect of correction for dwelling height on such exposure. The ARs with the highest population percentages exposed to concentrations above 300 Bq/m^3 were Galicia (14.1%), the Canary Islands (8.1%), and Extremadura (8.0%). Once correction for dwelling height was applied, this order was slightly inverted, with Galicia, Extremadura and the Canary Islands being the ARs with the highest population percentages exposed to more than 300 Bq/m^3, and the percentage of the population that was exposed becoming appreciably smaller (8.2%, 6.1%, and 5.3%, respectively).

Table 1
Prevalence of exposure to residential radon for each Autonomous Region, by radon concentration. Values shown uncorrected and corrected for dwelling height.

Autonomous Region	Uncorrected prevalences (%)			Corrected prevalences (%)		
	≤100 Bq/m^3	101–300 Bq/m^3	>300 Bq/m^3	≤100 Bq/m^3	101–300 Bq/m^3	>300 Bq/m^3
Andalusia	80.48	17.24	2.28	88.19	10.52	1.30
Aragon	80.29	17.41	2.31	90.86	8.18	0.96
Asturias, Principality of	79.02	18.08	2.89	91.19	7.71	1.10
Balearic Islands	80.68	17.19	2.14	88.52	10.3	1.17
Canary Islands	73.46	18.42	8.12	82.43	12.3	5.27
Cantabria	77.35	19,00	3.65	89.17	9.23	1.60
Castile & Leon	76.05	19.21	4.74	85.09	12.05	2.86
Castile-La Mancha	77.84	18.56	3.60	83.42	13.95	2.62
Catalonia	75.46	19.67	4.87	88.78	9.17	2.05
Valencian	81.46	16.76	1.78	91.72	7.58	0.71
Extremadura	71.32	20.69	7.99	77.63	16.26	6.12
Galicia	62.14	23.78	14.08	77.08	14.70	8.22
Madrid	78.65	18.12	3.23	92.75	6.26	0.99
Murcian	81.14	16.93	1.93	88.26	10.62	1.12
Navarre	80.48	17.31	2.2	91.06	8.05	0.90
Basque Country	79.47	17.84	2.69	94.32	5.06	0.62
Rioja, La	80.09	17.51	2.40	91.36	7.71	0.92
Ceuta	80.51	17.08	2.41	92.05	7.05	0.91
Melilla	81.48	16.75	1.77	91.35	7.94	0.71

The impact of correction for dwelling height on the prevalence of the exposed population was very marked in some ARs. The region where this impact was most evident was Madrid, where the population exposed to less than 100 Bq/m^3 went from 78.7% to 92.8%, after correction for dwelling height; similarly, in Galicia the population percentage exposed to more than 300 Bq/m^3 decreased from 14.1% to 8.2%.

3.1. Radon-attributable mortality corrected for dwelling height

In 2017, a total of 838 lung cancer deaths in Spain (3.8% of the total) were attributed to radon exposure. In men, Extremadura was the AR with the highest mortality rate, both crude and adjusted (11.24 cases and 11.46 cases per 100,000 inhabitants, respectively), followed by Galicia. In women, the AR with the highest rates was Galicia (2.37 and 2.12 cases per 100,000 inhabitants, respectively). Galicia was also the AR with the highest PAF (7.0%) (Table 2). The PAF was fourfold in the AR with the highest PAF compared to the lowest. The brunt of AM occurred among smokers and ex-smokers, both men and women (95.5%, 622 deaths and 74.2%, 119 deaths of the total, respectively).

3.2. Radon-attributable deaths without correction for dwelling height

In 2017, 1,533 deaths in population aged 35 years and over (1197 men and 336 women) can be attributed to residential radon exposure. This accounts for 6.9% of all lung cancer deaths in Spain. Broken down by AR, Galicia was the region that registered the highest percentage of deaths, followed by Extremadura and the Canary Islands. Galicia and Extremadura registered the highest radon-attributable mortality rates, both crude and adjusted, in men. Once again, the brunt of radon-

Table 3
Population attributable fractions (PAFs) in percentage, radon-attributable mortality (AM) due to lung cancer for each Autonomous Region and sex in 2017, overall and by tobacco use, in the population aged ≥ 35 years, and AM rate per 100,000 inhabitants. Data not corrected for dwelling height. Adjusted rates per age.

Autonomous Region	PAF(%)	Men						Women					
		Attributable mortality (AM)				AM rate by 10^5		Attributable mortality				AM rate by 10^5	
		Total	NS	ExS	S	Crude	Adjusted	Total	NS	ExS	S	Crude	Adjusted
Andalusia	6.05	178	7	76	95	7.21	8.32	39	12	7	20	1.47	1.47
Aragon	6.11	38	2	19	18	9.11	9.21	9	3	2	4	2.04	1.89
Asturias, Principality of	6.48	34	2	15	17	9.99	9.57	11	4	3	5	2.87	2.50
Balearic Islands	6,00	24	1	10	13	6.77	8.29	8	2	2	4	2.22	2.32
Canary Islands	8.04	54	2	23	29	8.02	9.77	19	5	4	11	2.79	2.96
Cantabria	6.95	18	1	9	8	9.88	10.25	6	2	1	3	3.00	2.76
Castile & Leon	7.32	77	3	40	34	9.43	8.72	21	8	4	9	2.39	2.05
Castile-La Mancha	6.81	57	3	26	28	9.15	9.80	11	5	1	5	1.72	1.64
Catalonia	7.49	194	8	91	94	8.62	9.43	58	21	15	23	2.38	2.28
Valencian	5.77	111	5	44	62	7.31	7.91	31	9	6	16	1.88	1.81
Extremadura	8.63	47	1	21	24	14.13	14.41	8	3	1	3	2.27	2.08
Galicia	11.08	136	8	63	65	15.32	14.54	37	15	8	15	3.75	3.35
Madrid	6.58	123	5	62	56	6.48	7.60	45	9	11	25	2.09	2.08
Murcian	5.86	27	1	11	15	6.35	7.67	7	3	1	3	1.51	1.54
Navarre	6.05	15	1	6	8	7.59	8.05	4	1	1	2	1.88	1.80
Basque Country	6.35	58	3	28	27	8.33	8.37	20	5	4	11	2.54	2.34
Rioja, La	6.17	6	0	3	3	5.97	6.08	2	1	0	1	1.59	1.46
Total	**6.96**	**1197**	**53**	**547**	**597**	**8.44**	**9.14**	**336**	**105**	**71**	**160**	**2.19**	**2.09**

AM: attributable mortality; ExS: ex-smokers; NS: never smokers; S: smokers.

attributable mortality occurred among smokers and ex-smokers (95.6%, 1,144 deaths in men and 68.8%, 231 deaths in women). The results broken down by AR, together with the crude and adjusted mortality rates and PAF, can be seen in Table 3.

Fig. 1 a and b depict the effect of correction for dwelling height on crude lung cancer mortality rates due to radon exposure in men and women, respectively. In some cases, these rates fell by more than half after adjustment for dwelling height. Fig. 2 shows the effect of correction for dwelling height on the PAF. In many ARs, this fraction fell by more than half. The impact was lower in those ARs where residential radon concentrations were highest (Galicia, Extremadura, and the Canary Islands). Radon-attributable mortality has a clear spatial pattern, as can be seen, and was higher in the two Castiles (i.e., Castile & León and Castile-La Mancha), Galicia, Extremadura, and the Canary Islands (Fig. 3). This same geographic pattern was observed for men and women alike (Fig. 3 a and b).

4. Discussion

The results of this study highlight that exposure to residential radon is an important cause of lung cancer mortality in Spain, causing 3.8% of all lung cancer deaths in 2017. The calculated PAF, uncorrected for dwelling height, would be 6.9% and hence upward biased. The impact of exposure to radon is highly variable, with Galicia and Extremadura being the most affected ARs, with radon causing 7% of all lung cancers deaths. These results are in line with those reported in other countries and justify legislation targeted at protecting the population from high residential radon concentrations. This is the first study to correct estimates of radon-attributable lung cancer mortality, by taking into account the fact that part of the population lives in dwellings situated on the upper floors of buildings. This adjustment is very important in order to not overestimate mortality attributable to this human carcinogen.

The AM to radon exposure obtained after applying the alternative method proposed by Gray et al. (2009) was similar. AM to radon

Table 2
Population attributable fractions (PAF) in percentage, radon-attributable mortality (AM) due to lung cancer for each Autonomous Region and sex in 2017, overall and by tobacco use, in the population aged ≥ 35 years, and AM rate per 100,000 inhabitants. Data corrected for dwelling height. Adjusted rates per age.

Autonomous Region	PAF(%)	Men						Women					
		Attributable mortality (AM)				AM rate by 10^5		AM				AM rate by 10^5	
		Total	NS	ExS	S	Crude	Adjusted	Total	NS	ExS	S	Crude	Adjusted
Andalusia	3.75	110	4	47	59	4.47	5.16	24	7	5	12	0.91	0.91
Aragon	2.93	18	1	9	9	4.37	4.42	4	1	1	2	0.98	0.91
Asturias, Principality of	2.83	15	1	7	8	4.36	4.18	5	2	1	2	1.25	1.09
Balearic Islands	3.65	14	1	6	8	4.12	5.05	5	1	1	2	1.35	1.41
Canary Islands	5.47	36	1	15	20	5.46	6.65	13	3	3	7	1.90	2.01
Cantabria	3.45	9	0	5	4	4.90	5.09	3	1	0	2	1.49	1.37
Castile & Leon	4.69	49	2	25	22	6.04	5.58	13	5	2	6	1.53	1.31
Castile-La Mancha	5.19	44	2	20	21	6.96	7.46	8	3	1	4	1.31	1.25
Catalonia	3.57	92	4	43	45	4.11	4.50	28	10	7	11	1.14	1.08
Valencian	2.66	51	2	21	29	3.38	3.65	14	4	3	7	0.87	0.84
Extremadura	6.87	37	1	17	19	11.24	11.46	6	3	1	3	1.80	1.65
Galicia	7.01	86	5	40	41	9.70	9.20	24	9	5	9	2.37	2.12
Madrid	2.34	44	2	22	20	2.30	2.70	16	3	4	9	0.74	0.74
Murcian	3.73	17	1	7	9	4.04	4.88	4	2	0	2	0.96	0.98
Navarre	2.87	7	0	3	4	3.60	3.81	2	0	0	1	0.89	0.85
Basque Country	1.84	17	1	8	8	2.42	2.43	6	1	1	3	0.74	0.68
Rioja, La	2.77	3	0	1	1	2.68	2.74	1	0	0	0	0.71	0.66
Total	**3.79**	**651**	**29**	**296**	**326**	**4.59**	**4.97**	**177**	**57**	**36**	**83**	**1.15**	**1.10**

AM: attributable mortality; ExS: ex-smokers; NS: never smokers; S: smokers.

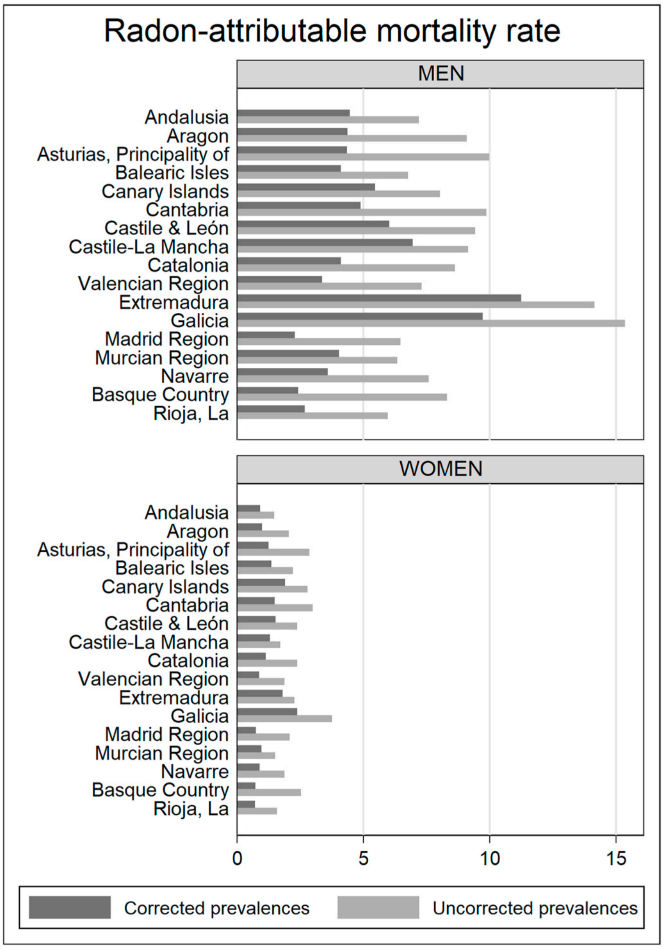

Fig. 1. Crude lung cancer mortality rate attributable to exposure to radon based on corrected and uncorrected exposure prevalence in men (a) and women (b). Rates per 100,000 inhabitants.

exposure accounted for 6.9% of the OM by lung cancer after applying the PAF-based methodology with uncorrected prevalence by height, whereas using Gray's methodology accounted for 7.5%. Differences arise when data were split by tobacco consumption. One of the main limitations of the results obtained by applying the PAF-based methodology is related to the distribution of AM as a function of the prevalence of tobacco consumption, since the results are conditioned by the prevalence applied.

In good measure, these results reflect both the geographic distribution of radon and population across the different parts of Spain. The ARs where exposure to residential radon is highest are: Galicia, the two Castiles, Extremadura, and the Canary Islands. In the Spanish case, it can be said that there is an inverse relation between population size and residential radon, since the most highly populated areas (Andalusia and the Mediterranean Basin) are those that register the lowest radon concentrations (with the exception of Madrid, where a good part of the population lives on the upper floors of apartment blocks). These distributions reflect the results observed at a national level, and reinforces the need for more local approaches to the control and reduction of exposure to residential radon, without excluding the necessity of analyzing specific geographic zones lying within areas classified as "low-risk".

The results observed in other countries vary widely, and indeed few countries have undertaken nationwide mortality-attribution studies. For instance, the study by Grundy et al. (2017), conducted in Alberta, Canada, yielded a high PAF (16.6%): this region registers a geometric mean of 71 Bq/m^3. Gaskin et al. estimated PAFs for different countries and found that the variability in the estimates is influenced, above all, by the mean radon concentration in the country in question (Gaskin et al., 2018). It should be noted, however, that this study was not adjusted for dwelling height and that much of the data on radon exposure at a national level was based on very few measurements. In the case of Spain, 5, 500 measurements were included in a study undertaken in 2014 (Sainz-Fernandez et al., 2014) as opposed to the 12,000 measurements included in ours. This makes for greatly improved radon estimates at a regional level, particularly in relatively large-sized countries like Spain. The greater part of lung cancer deaths due to radon exposure occur in smokers or ex-smokers, since there is a strong interaction between tobacco use and radon exposure (Lorenzo-Gonzalez et al., 2020; Health Risks of Radon). Although radon causes excess mortality in never

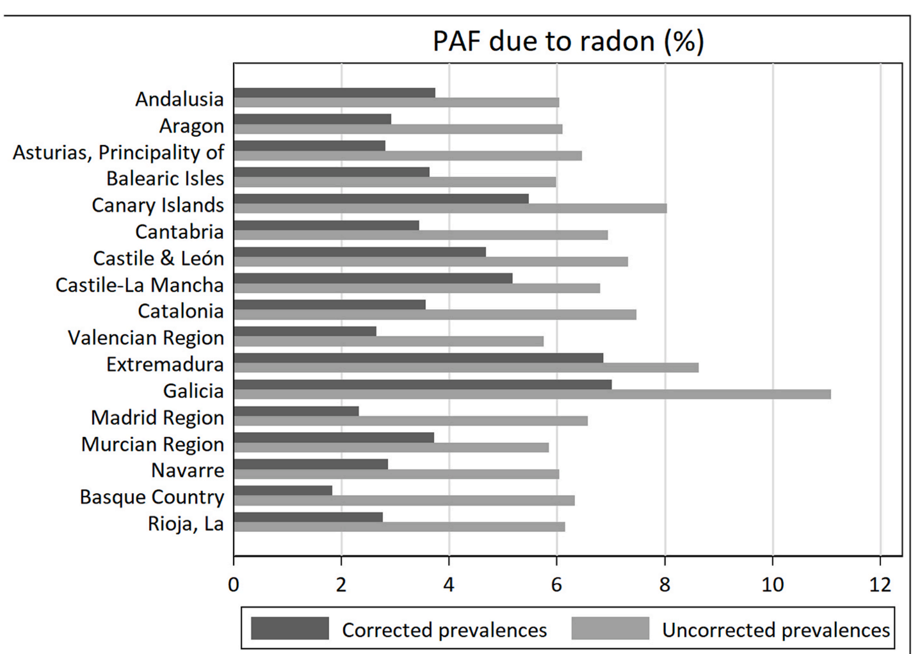

Fig. 2. Population attributable fraction of lung cancer mortality due to exposure to residential radon, according to correction for dwelling height.

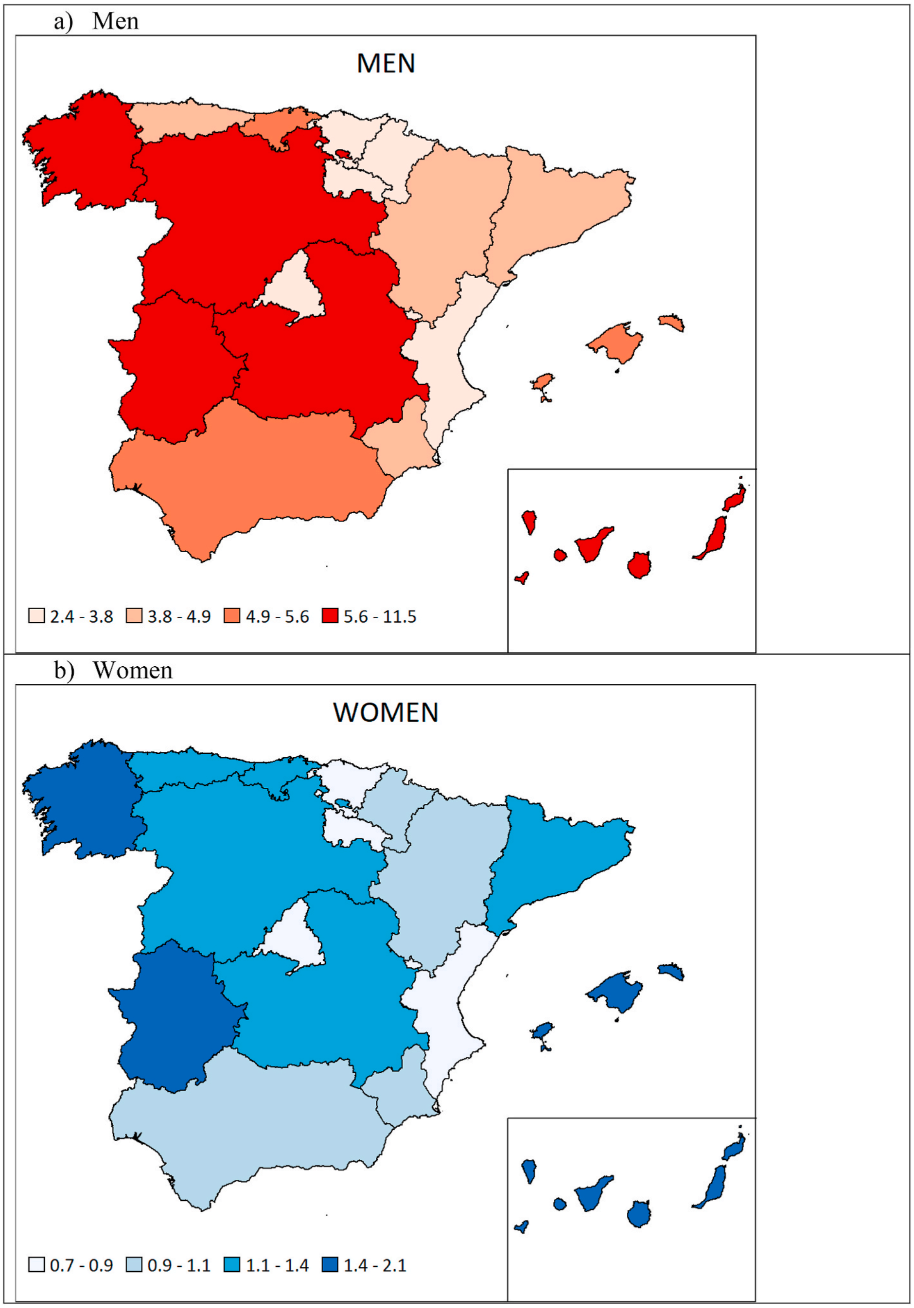

Fig. 3. Map by quartiles of the lung cancer mortality rate attributable to radon in men (a) and women (b). Adjusted rates per age per 100,000 inhabitants.

smokers, quantitatively speaking this is lower than that caused in ever smokers. Another study undertaken in Galicia observed that the greatest part of residential radon-attributable mortality occurs in smokers and ex-smokers, though this study was not adjusted for dwelling height and was based on around 400 radon measurements (Pérez-Ríos et al., 2010).

This study has limitations which can be described as those specific to mortality-attribution methods and to the quality and accuracy of the data sources. There are different methods of attributing lung cancer mortality to residential radon exposure. These methods range from adaptations of the standard mortality-attribution method based on exposure prevalence, across to data-intensive calculations based on mathematic modeling (reviewed in (Ajrouche et al., 2017)). Unfortunately, there is no standard method of choice, and this depends on data availability, both for radon but also on tobacco consumption. One of the main limitations of the results obtained by applying the PAF-based methodology is related to the distribution of AM as a function of the prevalence of tobacco consumption, since the results are conditioned by the prevalence applied. In addition to these differences in existing attribution methods is the fact that account must be taken of the population's tobacco use, since this is the leading lung cancer risk factor. This complicates estimates even further, because when lung cancer mortality due exclusively to tobacco use is estimated (Pérez-Ríos et al., 2010), other possible covariates are not taken into account, but when radon-attributable deaths are estimated, tobacco use must be included alongside radon exposure so as to be able to identify and distinguish the influence exerted by each of these risk factors on attribution.

Data used to estimate lung cancer mortality attributable to residential radon require that prevalence of smoking be representative of each AR by sex and age group; and the data in this study are representative, thanks to the availability of national surveys data (Ministerio de Sanidad, 2017; Ministerio de Sanidad and Servicios Sociales e Igualdad, 2011; Ministerio de Sanidad and Consumo y Bienestar Social, 2014). The radon-exposure prevalence data were sourced from the Nuclear Safety Council, and specifically from the Radon Potential Map of Spain (Consejo de Seguridad Nucl, 2019). These data correspond to a convenience sampling conducted in all Spanish provinces and autonomous cities in which radon concentrations were measured in homes situated on the ground and first floors. These data are representative of radon concentration at a national level. To correct population exposure prevalence for dwelling height, we used NSI Housing Census data (Instituto Nacional de Est, 2011), calculating the number of storeys above ground level for each province and applying a correction factor for exposure to radon. This made it possible to estimate the population exposure to residential radon, bearing in mind that not all the population lives on ground or first floors and therefore applying radon-concentration reduction factors for dwelling height. Data on the strength of association between tobacco use and lung cancer in the population aged 35–54 years were obtained from the follow-up of the Cancer Prevention Study II (CPS-II): this is the study with the largest sample size and longest follow-up time published to date on tobacco use and lung cancer risk (National Center for Chron, 2014), thereby making it the best evidence available for assessing excess risk of tobacco-related deaths. In the population over the age of 54 years, the relative risks were derived from the joint analysis of the follow-up of five large cohorts, including the CPS-II. For risk of lung cancer due to residential radon, we used one of the largest studies with data on radon and lung cancer from a single country, which was published in 2020 and undertaken in the northeast of Spain (Lorenzo-Gonzalez et al., 2020). This study included around 4,000 participants and can be regarded as correctly representing the residential habits of the Spanish population. The fact that it was fundamentally conducted in risk areas makes it easier to obtain dose-response associations that can be applied to areas/dwellings which may also have these high radon concentrations. The results of this calculation only indirectly take into account the properties of residential building materials, by the use of representative radon-concentration measurements. Radon readings for this study were obtained by the Galician Radon Laboratory (www.radon.gal), an accredited lab with extensive experience on indoor radon measurements.

The advantages of our study include having detailed data at a national level for drawing up all the estimates, as well as the possibility of applying the correction described above for dwelling height in the estimation of radon-attributable mortality in Spain, which is a completely novel approach.

To conclude, elevated radon exposure is the cause of death for 1 out of 26 lung cancer patients (3.8%), in Spain. Even so, the impact on mortality is very uneven, depending on the AR in question. The most affected regions are Galicia and Extremadura, which account for 7% of all lung cancer deaths attributable to radon exposure. The greater part of lung cancer deaths due to radon exposure occur among smokers and ex-smokers. Lastly, correction of radon exposure for dwelling height attenuates radon-attributable deaths to a major extent and should be considered in all studies that seek to quantify the impact of exposure to radon on lung cancer mortality. These data should serve to support decision-making by national and regional health authorities when it comes to promoting measures that would protect the population and workers from high residential radon concentrations.

Credit author statement

A Ruano-Ravina had the original idea and designed the research methodology. A Ruano-Ravina, Mónica Pérez-Ríos and Marta García-Talavera decided how to implement radon exposure in the estimation methods. Marta García-Talavera, María Isolina Santiago-Pérez and Mónica Pérez-Ríos decided the statistical modeling and tested the sensitivity analysis. All authors have provided intellectual input to the content of the manuscript and approved the first draft. All authors have read the final version of the manuscript and have approved it. All authors take public responsibility on the content of the manuscript.

Declaration of competing interest

The authors do not have any conflict of interest.

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Directorate-General of Public Health, Ministry of Health, Spain. The Ministry of Health had no role in defining the methodology or in obtaining or interpreting the results. A full version of this study will be published in Spanish by the Spanish Ministry of Health.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.envres.2021.111372.

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