



## Mini-review

Residential radon and lung cancer in never smokers. A systematic review <sup>☆</sup>María Torres-Durán <sup>a,b</sup>, Juan Miguel Barros-Dios <sup>a,c,d</sup>, Alberto Fernández-Villar <sup>b</sup>, Alberto Ruano-Ravina <sup>a,c,\*</sup><sup>a</sup> Department of Preventive Medicine and Public Health, University of Santiago de Compostela, Spain<sup>b</sup> Service of Neumology, University Hospital Complex of Vigo, Spain<sup>c</sup> CIBER de Epidemiología y Salud Pública, CIBERESP, Spain<sup>d</sup> Service of Preventive Medicine, University Hospital Complex of Santiago de Compostela, Spain

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## ABSTRACT

Radon exposure is considered the second cause of lung cancer and the first in never smokers. We aim to assess the effect of residential radon exposure on the risk of lung cancer in never smokers through a systematic review applying predefined inclusion and exclusion criteria. 14 Studies were included. Some of them point to a relationship between residential radon and lung cancer while others show no association. Further studies are necessary to test this association and to assess if other risk factors such as environmental tobacco smoke could modify the effect of residential radon exposure on lung cancer.

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## 1. Introduction

Lung cancer is the first cause of cancer mortality in the World, with more than 1,400,000 annual deaths [1,2]. Tobacco consumption is its main risk factor, and between 10% and 25% of all lung cancer cases occur among never smokers [3]. Though at first sight it could seem a low percentage, if we consider lung cancer in never smokers as a specific cancer it would rank the seventh cause of cancer death worldwide [4]. Many authors state that lung cancer in never smokers should be considered as a different disease than lung cancer due to tobacco consumption [4–6]. Residential radon exposure is the second cause of lung cancer after tobacco consumption and it is the main risk factor among never smokers [7]. It is estimated that radon exposure could play a role in 30% of lung cancer deaths occurred in never smokers [8].

Many countries have depicted residential radon exposure maps in order to characterize those areas with the highest indoor radon concentrations. The Environmental Protection Agency (USA)

established in 1987 148 Bq/m<sup>3</sup> as the action level [9] and the World Health Organization has recently lowered the recommended levels below 100 Bq/m<sup>3</sup> [7]. WHO recommendation is based on the results of the two most relevant studies regarding residential radon and lung cancer performed in Europe and North America, respectively [10,11].

Both studies observed a linear and statistically significant increase on the risk of lung cancer with residential radon exposure.

Despite of this evidence there are scant studies on residential radon and lung cancer performed exclusively in never smokers. Among the published investigations we should highlight a Swedish study [12] which included never smokers from 5 different case-control studies. This study observed a relative risk of 1.44 (95%CI 1.0–2.1) for those exposed to concentrations higher than 140 Bq/m<sup>3</sup> compared with those exposed to concentrations lower than 50 Bq/m<sup>3</sup>. This is one of the three available studies performed exclusively in never smokers [13,14]. The other published studies did not make a difference between smokers and never smokers or the subgroup of never smokers had a very low sample size when it was analyzed independently.

Taking into account the importance of residential radon as a risk factor for lung cancer and the limited and fragmented available evidence for never smokers, we aim to assess the effect of residential radon exposure on lung cancer risk in never smokers through a systematic review of the published literature.

<sup>☆</sup> This work is part of the research conducting to the PhD degree of María Torres Durán, MD.

\* Corresponding author. Address: Department of Preventive Medicine and Public Health, School of Medicine, C/San Francisco s/n, University of Santiago de Compostela, 15782 Santiago de Compostela, Spain. Tel.: +34 881 812267; fax: +34 881 872282.

E-mail address: [alberto.ruano@usc.es](mailto:alberto.ruano@usc.es) (A. Ruano-Ravina).

**Table 1**  
Quality scale used to assess the included studies.

Item assessed	Characteristic	Weight
Total sample size	200–500	0
	501–1000	1
	>1000	2
Number of never smoking cases	50–150	0
	151–400	1
	>400	2
Covariables adjustment (number)	2 (Age and gender)	0
	>2	2
Study design	Hospital-based case-control study	0
	Population-based case-control study	1
	Cohort study	2
	Pooling study	3
Radon measurements	Not specified or charcoal	0
	Alpha-track or other	1
Total		10

## 2. Methods

### 2.1. Literature search

We performed a literature search in Pubmed (Medline) and EMBASE. To retrieve information we used a predefined search strategy employing keywords (radon; lung neoplasms; never smokers; systematic review) complemented with free text. We also searched in the databases of the Center for Reviews and Dissemination (CRD databases) of the York University and on the Cochrane Library. The search period comprised between the first of January 1985 and 31st of December 2012. We used as search languages English, Spanish and French.

### 2.2. Inclusion and exclusion criteria

We used the following inclusion and exclusion criteria to include papers in the systematic review: (a) regarding the study design we included: cohort studies, case-control studies, systematic reviews or meta-analysis; (b) regarding the participants' characteristics we included only studies performed on general population; (c) regarding radon measurements we included studies that placed a radon detector in the dwellings of participants; (d) regarding the sample size we included only those studies with at least 50 never smoking lung cancer cases and the overall sample size had to be higher than 200 individuals; (e) regarding lung cancer diagnosis,

only studies with anatomopathological diagnosis were included and, finally, and (f) studies that did not differentiate the results for smokers and never smokers were excluded.

The definition of never smoker was the fulfillment of at least one of these conditions: participants have never smoked more than 100 cigarettes in a lifetime or less than 1 cigarette per 6-months period during lifetime.

We retrieved the same information for each of the included papers (following the PRISMA guidelines, [www.prisma-statement.org](http://www.prisma-statement.org)) using a standardized procedure. We have presented information from each study in an evidence table and a global qualitative conclusion has been reached. To perform a meta-analysis has not been possible due to the high heterogeneity of the included studies.

### 2.3. Assessment of the study quality

The full text of the included papers was read by two reviewers (MTD and ARR). Discrepancies in data interpretation were resolved by consensus. To assess the quality of each of the included studies we designed a quality scale with 5 items which scored characteristics of the included papers. These items were: sample size, number of never smoking lung cancer cases, results adjusted by covariables, study design, and method of radon concentration assessment. We have given different weights to these characteristics allowing us to create a continuous scale. The scale with the weighting of each item appears in [Table 1](#).

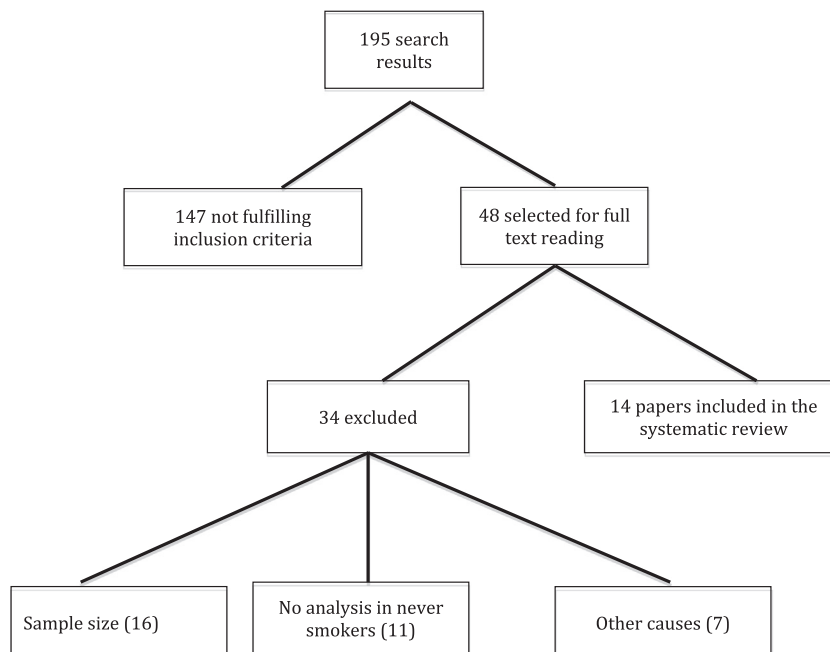
## 3. Results

### 3.1. Search results

We obtained 195 papers through the literature search. After reading all the abstracts we selected 48 for full text reading. Of them, 14 finally fulfilled the established inclusion criteria. Among them, we included the European and North American pooling studies (with two publications each one), a cohort study and nine case-control studies. Most of the investigations were performed in Europe and North America. Individual studies had a sample size ranging between 56 and 844 never smokers. The most common exclusion criteria were: sample size below 50 never smoking cases and that the analysis did not differentiate the results between never and ever smokers. A description of the search process appears in [Fig. 1](#).

### 3.2. Results of the included studies

The most prominent studies published to date have been two pooling studies, one based on 13 European case-control studies



**Fig. 1.** Flowchart showing inclusion and exclusion flow.

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