Int. J. Environ. Sci. Technol. (2013) 10:891–902
DOI 10.1007/s13762-013-0248-6

ORIGINAL PAPER

Lung cancer risk associated with residential proximity to industrial installations: a spatial analysis

M. F. López-Cima · J. García-Pérez · B. Pérez-Gómez · N. Aragonés · G. López-Abente · T. Pascual · A. Tardón · M. Pollán

Received: 6 November 2011 / Revised: 25 March 2012 / Accepted: 16 April 2012 / Published online: 12 April 2013

Abstract Lung cancer is the most common cause of cancer-related death and thus a major public health problem. While lung cancer frequency might be partially attributable to smoking habit and occupational exposure, the role of industrial pollution also needs to be assessed. To ascertain the possible effect of residential proximity to industrial installations on lung cancer risk in Asturias, an industrial region in Spain, taking into account the type of industrial activity and carcinogenic substances released. We conducted a hospital-based case–control study covering 700 lung cancer patients and 700 controls recruited in Asturias, matched individually by ethnicity, hospital, age, and sex. Distances were computed from the respective participants' residential locations to the 48 industrial facilities governed by the Integrated Pollution Prevention and Control Act 16/2002 and included in the European Pollutant Release and Transfer Register, and located in the study areas. Using logistic regression, odds ratios (ORs) and 95 % confidence intervals (95 % CIs) were calculated and adjusted for sex, age, hospital area, tobacco consumption, family history of cancer, area of residence, and occupation. Excess risk of lung cancer was observed for individuals living near industrial installations (OR = 1.43; 95 % CI = 1.08–1.89), particularly metal industries (OR = 1.40; 95 % CI = 1.05–1.87), cement plants (OR = 4.81; 95 % CI = 1.20–19.19), and shipyards (OR = 1.69; 95 % CI = 1.17–2.43). Residents living close to industrial facilities releasing dioxins displayed a high, though non-statistically significant, excess risk of lung cancer (OR = 1.62; 95 % CI = 0.86–3.07). This study suggests a possible association between lung cancer risk and proximity to industrial installations, specifically metal industries, cement plants, and shipyards.

Keywords Industrial pollution · Industries · Case–control study · Lung cancer

M. F. López-Cima and J. García-Pérez contributed equally to this study.
A. Tardón and M. Pollán contributed equally to the design of the study.

M. F. López-Cima (✉) · J. García-Pérez · B. Pérez-Gómez · N. Aragonés · G. López-Abente · M. Pollán
Cancer and Environmental Epidemiology Unit, National Center for Epidemiology, Carlos III Institute of Health, Avda. Monforte de Lemos, 5, 28029 Madrid, Spain
e-mail: flcina@isciii.es

M. F. López-Cima · J. García-Pérez · B. Pérez-Gómez · N. Aragonés · G. López-Abente · A. Tardón · M. Pollán
CIBER en Epidemiología y Salud Pública (CIBERESP), Madrid, Spain

M. F. López-Cima · A. Tardón
Molecular Epidemiology of Cancer Unit, University Institute of Oncology, University of Oviedo, C/Fernando Bongera, s/n, 33006 Oviedo, Spain

T. Pascual
Pneumology Department, Cabueñes Hospital, Cabueñes, s/n, 33394 Gijón, Spain

Introduction

Lung cancer is the most common cause of cancer-related death and thus a major public health problem (Ferlay et al. 2010). In Spain, it accounted for more than 20,000 deaths in 2008, which amounted to 27 % of all cancer deaths in males and 8 % in females (Área de Epidemiología Ambiental y cáncer—Centro Nacional de Epidemiología—ISCIII 2013).

Although cigarette smoking is the main risk factor for lung cancer (IARC 1986), there are other well-known lung carcinogens, such as occupational exposure to a number of substances, including arsenic, asbestos, chromium, cadmium, and nickel (Clapp et al. 2005), or environmental exposure to radon (Catelinois et al. 2006) or air pollution (Raaschou-Nielsen et al. 2011). Other factors too, such as low intake of fresh fruit and vegetables, have been related with higher risk of lung cancer (Gonzalez and Riboli 2010).

In addition, several studies have reported an association between risk of lung cancer and proximity to certain industries releasing carcinogenic substances into the environment, such as combustion installations (Garcia-Perez et al. 2009), iron and steel foundries (Pless-Mulloli et al. 1998; Smith et al. 1987), chemical industries (Pless-Mulloli et al. 1998), petrochemical plants (Belli et al. 2004), coke oven plants (Parodi et al. 2005), incinerators (Barbone et al. 1995) and sewage plants (Pizzo et al. 2011). Consequently, the public health relevance of a possible relationship between environmental exposure to industrial installations and lung cancer makes it a research area of great interest.

In a previous study, our group furnished preliminary evidence of the possible role of residential proximity to both urban and industrial areas as a moderate risk factor for lung cancer (Lopez-Cima et al. 2011), based on the results of the ongoing, hospital-based, case–control *CAPUA* (*CÁncer de PUlmon en Asturias*—Lung Cancer in Asturias) study (Marin et al. 2004), targeting a highly industrialized region in Spain. The present paper now analyzes the effects of exposure to specific industrial sectors and/or carcinogenic substances on lung cancer risk within the context of the *CAPUA* study (Spanish region of Asturias, 2000–2009), by incorporating updated information on industries from both the Integrated Pollution Prevention and Control (IPPC) Register and the European Pollutant Release and Transfer Register (E-PRTR), and taking advantage of the higher statistical power resulting from the increase in the number of cases and controls included in the study by the end of recruitment.

Materials and methods

Study subjects

The *CAPUA* study is a hospital-based case–control study conducted by the Molecular Epidemiology of Cancer Unit at the University Institute of Oncology (University of Oviedo). Details of the study design and methods have been described elsewhere (Fernandez-Rubio et al. 2008; Gonzalez-Arriaga et al. 2008; Leader et al. 2010; Lopez-Cima et al. 2007; Marin et al. 2004). Briefly, patients were recruited at four public hospitals in Asturias, each of which is the referral center for the surrounding health catchment area (i.e., the respective administrative health division). The four hospitals were: the Cabueñes Hospital in the city of Gijon (263,457 inhabitants in 2010); the San Agustin Hospital in the town of Aviles (79,105 inhabitants); the General Hospital in the city of Oviedo (209,549 inhabitants); and the Alvarez-Buylla Hospital in the town of Mieres (24,735 inhabitants) (Sociedad asturiana de estudios económicos e industriales (sadei) 2011). Each hospital attends to the residents of its designated catchment area, which includes the relevant host town or city, plus all smaller outlying municipalities coming within the geographic boundaries defined by the health authorities. In the period October 2000 through December 2009, a standard protocol was used to recruit a total of 884 incident cases of histologically confirmed lung cancer, along with 772 controls individually matched to cases by ethnicity, hospital, sex, and age ($\pm$5 years). Controls were selected from among patients admitted to hospitals for acute health conditions unrelated to tobacco consumption. The most frequent diseases or conditions of controls were as follows: 35.9 %, inguinal or abdominal hernias [International Classification of Diseases-9th revision (ICD-9): 550–553]; 29.7 %, injuries (ICD-9: 800–848, 860–869, 880–897); and 12.4 %, intestinal obstructions (ICD-9: 560, 569, 574). Both cases and controls were required to reside within the recruiting hospital's designated geographic health area. The study was approved by the ethics committees of the corresponding hospitals, and written consent was obtained from all participants.

Data-collection

Information on known or potential risk factors for lung cancer was personally collected by trained interviewers using computer-assisted questionnaires, during patients' first hospital admission for diagnosis. Structured questionnaires were used to gather data on each participant's age, sex, sociodemographic characteristics, residential history (including address of last residence), current and past tobacco use, personal and family history of cancer, and occupational history.

Participants were categorized by tobacco consumption into three groups, namely: never smokers, defined as subjects who had not smoked at least one cigarette per day regularly for 6 months or longer in their lifetimes; former smokers, defined as regular smokers who had stopped smoking at least 5 years before the interview; and current smokers, defined as subjects who met none of these criteria. Smoking intensity [pack-years (PY)] was defined as the number of packs of cigarettes smoked per day multiplied by the number of years of smoking. Subjects were also categorized as light ($<$38 PY) or heavy ($\geq$38 PY) smokers, based on mean cumulative tobacco consumption in the control group. Finally, smoking status and intensity were combined into a joint variable having the following five levels: never smokers; former smokers <38 PY; current smokers <38 PY; former smokers ≥38 PY; and current smokers ≥38 PY.

For each job held for a minimum of 6 months or longer, we obtained information on industry name, production type, job title, and the years in which the job began and ended. Occupations and industries were coded using the 1977 Standard Occupational Classification (Office of Federal Statistical Policy and Standards 1977) and 1972 Standard Industrial Classification schemes (Office of Federal Statistical Policy and Standards 1972). Lastly, each coded occupation was categorized as a high-risk or non-high-risk occupation for lung cancer in accordance with published literature. Hence, to study occupational history, participants were classified into three groups, namely, unexposed individuals who had never worked in a high-risk job, subjects who had worked <37 years in a high-risk job, and finally, subjects who had worked ≥37 years in a high-risk job. This cut-off was based on the 80th percentile of time spent in high-risk jobs by the control group.

Geographic analysis

Each participant's last residence was geocoded using BatchGeo (Batchgeo 2013) and the Spanish Farm Plot Geographic Information System (*Sistema de Información Geográfica de Parcelas Agrícolas—SIGPAC)* (Ministerio de Medio Ambiente y Medio Rural y Marino 2011). To measure distances, a geodesic calculator was used to convert BatchGeo WGS84-projection coordinates (longitude/latitude) into the Universal Transverse Mercator (UTM) Zone 30 (ED50) coordinates used by *SIGPAC*.

Of the 1,656 participants interviewed (884 cases and 772 controls), 1,573 individuals' residences (857 cases and 716 controls) were geocoded, 1,300 using BatchGeo and 273 using *SIGPAC*. A total of 157 cases without matched controls and 16 controls without matched cases were excluded from the analyses (these persons had characteristics similar to those included in the study). Consequently, the final study population comprised 700 matched pairs, all of whom were Caucasian.

We used data on industries governed by the IPPC, Directive 96/61/CE and Act 16/2002 enacted by the European Commission (European Commission Environment 2012), and facilities pertaining to industrial activities not subject to the IPPC Act 16/2002 but included in the E-PRTR. The IPPC Act incorporates the above Directive into the Spanish legal system, and lays down that, in order to be able to operate, industries covered by the regulation must obtain the so-called Integrated Environmental Permit. We analyzed the industrial database (IPPC + E-PRTR) provided by the Spanish Ministry for the Environment and Rural and Marine Habitats for 2007, which includes information on the geographic location and industrial pollution emissions of all industrial plants in Spain. To take a minimum induction period of 10 years into account, in line with recommendations for solid tumors (Armenian and Lilienfeld 1974), we identified a total of 48 industrial installations in the health areas targeted, which had gone into operation prior to 1995 (10 years before the mid-point of the recruitment period, 2000–2009) and had reported releases to air in 2007, along with the previously validated geographic coordinates of their respective locations (Garcia-Perez et al. 2008). Data on the date of commencement of industrial activity were obtained from the official websites of the industrial companies themselves. These 48 installations were classified according to type of industrial sector, as follows: energy industry—combustion installations—(IPPC category-1); metal industry (IPPC category-2), including steel production and founding, galvanizing, ferrous metal foundries, non-ferrous metal smelters and producers (aluminum, zinc, copper), and surface treatment using an electrolytic or chemical process; mineral industry (IPPC category-3), including mining, production of cement, and production of glass and ceramic; chemical industry (IPPC category-4); waste and wastewater management (IPPC category-5); textile industry (IPPC category-7); food and beverage sector (IPPC category-9); and shipyards (E-PRTR category-9.e).

For each subject, the following Euclidean distances were calculated: (a) industrial distance, i.e., the distance between the subjects last residence and any of the previously mentioned 48 industrial installations (using a purpose-designed distance matrix between all industrial facilities and subjects); and (b) urban distance, i.e., the distance between the subject's last residence and the centroid of the town in which the hospital was situated.

For each subject, the exposure variable was coded as follows:

(a) residence in an industrial area, defined in terms of proximity to industrial facilities. The following distances were considered: 5, 4, 3, 2.5, and 2 km;
(b) residence in the urban area, taking, as in the previous report (Lopez-Cima et al. 2011), the area defined by the first decile of urban distance among controls; and,
(c) residence within the reference area, consisting of zones not included above and corresponding mainly to rural settings.

Data analysis

Since matching conditions, i.e., sex, age and hospital area, are very general, and controls can fit the criteria for more than one case (the corresponding pairs can be interchangeable), unconditional logistic regression models were used to estimate odds ratios (ORs) and 95 % confidence intervals (95 % CIs), to assess the relationship between lung cancer and proximity to any industrial installation (taking various above-defined industrial distances into account). All models included matching variables and other potential confounders, such as smoking, occupation, residence in the urban area, and family history of cancer (classified into three levels, i.e., none, first-degree relatives with cancer originating in an organ other than lung, and first-degree relatives with lung cancer).

In a second phase, we evaluated the relationship between lung cancer and industrial proximity by industrial sector and, in particular, by industrial facility, using the above-described multiple unconditional logistic regression model for the industrial distance which yielded the highest OR.

Lastly, we assessed the relationship between lung cancer and residential proximity to any focus releasing substances, or industrial activities classified by the International Agency for Research on Cancer (IARC) as carcinogens in humans and related to lung cancer (IARC 2012). For this purpose, the industrial distance chosen in the second phase was used to define an "exposed subject" as any person who lived close to any of the following carcinogens/carcinogenic facilities:

(a) arsenic–cadmium–chromium (these exposures could not be separated because 93 % of the facilities involved, released all three);
(b) nickel or nickel compounds;
(c) dioxins and furans;
(d) aluminum production, including industrial facilities devoted to this;
(e) iron and steel founding; and,
(f) shipyards.

For the purposes of this model, we included a variable identifying people living close (by reference to the industrial distance defined in the second phase) to other IPPC industrial facilities unrelated with the above-mentioned industrial activities and pollutants. The reference area consisted of zones not included above, and corresponded mainly to rural settings.

Results and discussion

The analysis covered 700 lung cancer cases and 700 controls drawn from the Caucasian population of Asturias. Distribution by sex, age, hospital area, smoking history (smoking status, smoking intensity, and tobacco consumption), family history of cancer, occupational history, and time of residence in last abode is summarized in Table 1. There were more current smokers (61.9 vs. 33.3 %) and more heavy smokers (61.18 vs. 37.91 PY) among cases than controls ($P < 0.001$).

Locations of 48 industrial installations, town centroids of the hospitals targeted, and residences of cases and controls are depicted in Fig. 1.

Estimated ORs associated with residential proximity to industrial installations using different distances are shown in Table 2. An increased risk of lung cancer was observed for all distances analyzed, with this proving higher and statistically significant for residents living within 3 km of industrial facilities (adjusted OR = 1.43; 95 % CI = 1.08–1.89). As a result, this distance was used to define industrial proximity in subsequent analyses. Lastly, intersection between industrial and urban areas using 3 km as the critical distance was also statistically significant (adjusted OR = 1.55; 95 % CI = 1.00–2.40).

Estimated ORs of lung cancer, both overall and by industrial sector, are shown in Table 3. When type of industrial activity was taken into account, all industrial sectors in the study area—with the exception of mining, non-ferrous metal smelters and producers, and iron founding—showed an increased risk of lung cancer, with this reaching statistical significance in the case of the metal industry (adjusted OR = 1.40; 95 % CI = 1.05–1.87) and the galvanizing sub-sector in particular (adjusted OR = 1.66; 95 % CI = 1.18–2.33), cement plants (adjusted OR = 4.81; 95 % CI = 1.20–19.19), and shipyards (adjusted OR = 1.69; 95 % CI = 1.17–2.43).

Table 4 shows the estimated ORs of lung cancer for facilities having a large enough population within a radius of 3 km (number of cases + controls >5 and number of cases >0, in every case). Individuals living in the vicinity of the only facility belonging to the energy sector showed a non-statistically significant increased risk of lung cancer. Individuals living within 3 km of seven metal industries (including three galvanizing complexes, two surface-treatment installations, one steel manufacturing plant and one aluminum production facility) registered an increased risk of lung cancer, with this reaching statistical significance in the case of two of the galvanizing plants (PRTR codes "1948" and "3096") (adjusted OR = 1.74; 95 % CI = 1.04–2.89 and adjusted OR = 1.79; 95 % CI = 1.24–2.59, respectively). An increased risk of lung cancer was also found for individuals living in the vicinity of four registered mineral industries, one devoted to cement production and three to glass and ceramics. Similarly, residents living close to two chemical industries, one a waste management facility and the other a textile plant, displayed a non-significant increased risk of lung cancer. Finally, subjects residing close to the shipyard registered a statistically significant excess risk of lung cancer (adjusted OR = 1.69; 95 % CI = 1.17–2.43).

Table 1 Characteristics of lung cancer cases and controls

Characteristics	Cases ($N = 700$) N (%)	Controls ($N = 700$) N (%)	P^a
Sex			
Male	604 (86.3)	604 (86.3)	
Female	96 (13.7)	96 (13.7)	1.000
Age (years), mean (SD)	65.28 (11.17)	64.28 (11.30)	0.098
Hospital area[b]			
Gijon (Cabueñes Hospital)	422 (60.3)	422 (60.3)	
Aviles (San Agustin Hospital)	178 (25.4)	178 (25.4)	
Oviedo (General Hospital)	58 (8.3)	58 (8.3)	
Mieres (Alvarez-Buylla Hospital)	42 (6.0)	42 (6.0)	1.000
Smoking Status			
Never	56 (8.0)	212 (30.3)	
Ever	644 (92.0)	487 (69.7)	<0.001
Former	211 (30.1)	254 (36.4)	
Current	433 (61.9)	233 (33.3)	<0.001
PY[c], mean (SD)	61.18 (35.72)	37.91 (31.87)	<0.001
Smoking			
Never	56 (8.1)	212 (30.9)	
Former < 38 PY	74 (10.7)	172 (25.1)	
Current < 38 PY	81 (11.7)	108 (15.7)	
Former ≥ 38 PY	135 (19.5)	76 (11.1)	
Current ≥ 38 PY	346 (50.0)	118 (17.2)	<0.001
Family history of cancer			
None	387 (57.8)	412 (59.6)	
Other cancers	206 (30.8)	231 (33.4)	
Lung cancer	76 (11.4)	48 (7.0)	0.083
Worker in high-risk occupation			
Never	247 (35.6)	268 (38.5)	
Ever	447 (64.4)	429 (61.5)	0.270
Time in high-risk occupation[d], mean (SD)	26.17 (14.52)	24.44 (13.85)	0.072
Population living in their last residence			
For more than 5 years	619 (90.0)	621 (90.0)	0.943
For more than 10 years	559 (81.3)	563 (81.6)	0.924

[a] Two-sided Chi-square test, and Mann–Whitney test where appropriate

[b] Hospital area refers to each hospital's health catchment area

[c] Pack-years for ever-smokers

[d] Time (in years) for ever-workers

Table 5 shows the estimated ORs of lung cancer by reference to carcinogens released or type of industry classified by the IARC as a group 1 carcinogen. Areas with exposure to arsenic, cadmium and chromium were analyzed jointly, since these pollutants were released by virtually the same facilities (see Table 6); in fact, 93 % of the population exposed to arsenic was also exposed to cadmium and chromium. Residents living close to industrial facilities releasing nickel or dioxins displayed a non-statistically significant excess risk of lung cancer, with this being especially high for industries releasing dioxins (OR = 1.59, 95 % CI = 0.84–3.01). As indicated above, the shipyard—deemed carcinogenic due to its use of asbestos and so included in our analysis—registered a statistically significant increased risk of lung cancer.

We set out to examine the effects of exposure to industrial air pollution on lung cancer risk in an industrialized area of Northern Spain, taking into account different industrial sectors and carcinogenic substances or activities. Our findings support the hypothesis that living in the proximity (≤3 km) of industrial installations might be a risk factor for lung cancer incidence. Indeed, our analyses show an excess of risk of lung cancer among residents in the proximity of industrial facilities, especially those living near metal industries, cement plants, and shipyards.

This paper takes an in-depth look at the same line of research as our previous report (Lopez-Cima et al. 2011), which analyzed lung cancer risk with regard to residential proximity to urban nuclei and industrial areas. This study benefited from an increased number of cases and controls, and furnished type-specific risks by industrial sector and carcinogenic substance. It is one of the first studies of its kind to use IPPC- and E-PRTR-based information to explore the effects in terms of cancer risk, attributable to pollution emitted by specific industrial sectors and/or carcinogenic substances. Unlike ecological approaches, our study design guarantees the availability of individual information on potential confounders, such as other lung cancer risk factors like smoking habit and occupational exposure, which can thus be controlled for in the analysis.

Insofar as environmental exposure is concerned, our measures were based on participants' residential location; and although we were only able to take the geographical coordinates of subjects' last-reported residence into account, our study population nevertheless proved to be very stable, with 90.0 % of cases and 90.0 % of controls having lived in their last-reported residence for more than 5 years, and 81.3 % of cases and 81.6 % of controls having lived there for more than 10 years. Moreover, a sensitivity analysis considering only long-term residents was conducted and yielded similar results (data not shown). Geocoding of place of residence affords relevant advantages for a case–control study, in that recall bias could not be expected to have any influence. The recruitment of incident cases also served to prevent possible changes of address associated with diagnosis of cancer. Hence, if there were any bias affecting proximity to pollution sources in

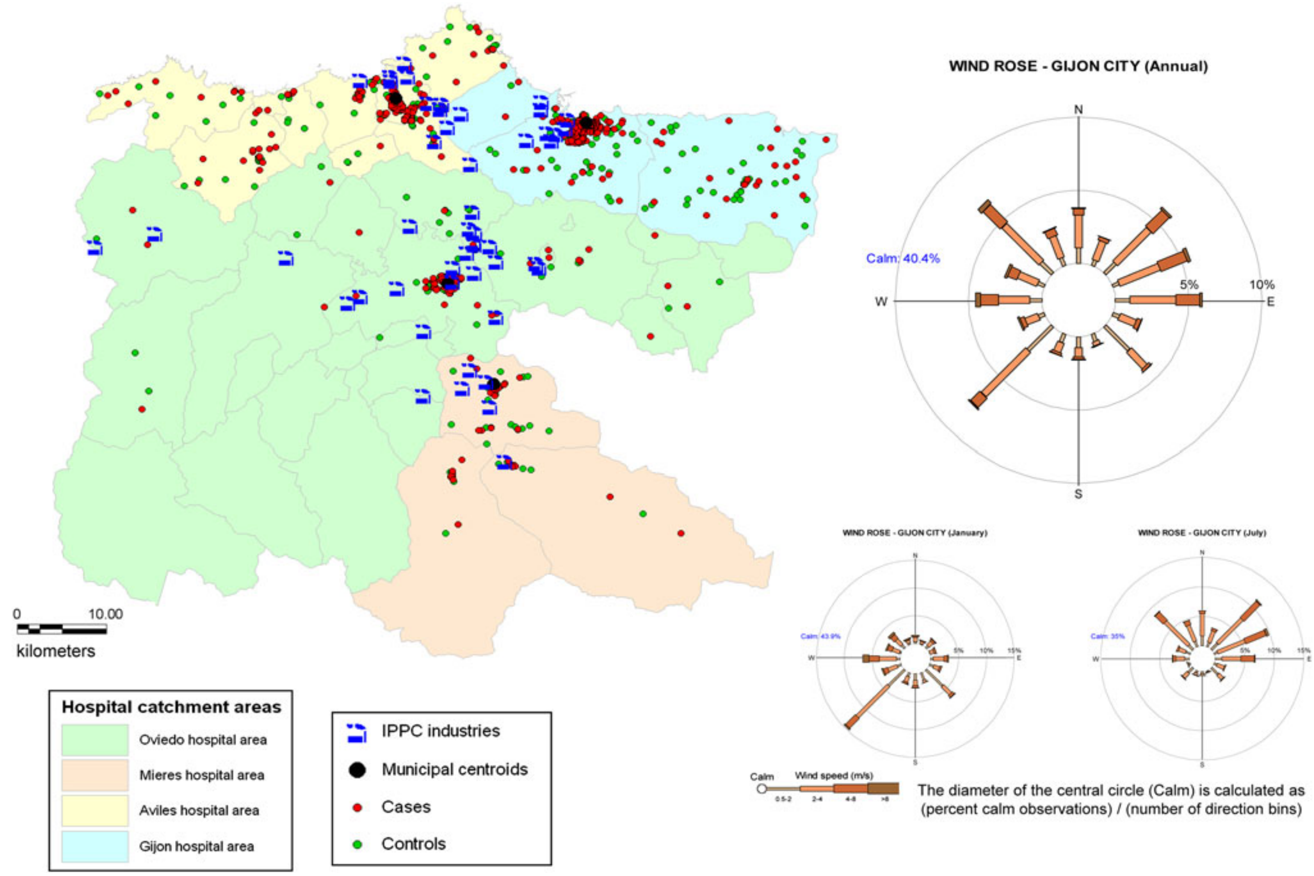

Fig. 1 Geographic distribution of cases, controls, industrial installations, and centroids in the four health areas and wind roses for the city of Gijon, for the period 1971–2000 (annual, January, and July)

relevant periods of life, our bias would be non-differential, causing an attenuation of the estimated effect.

Distance was used as a surrogate of environmental exposure to industrial emissions. Yet, the extent and dispersion of air emissions are critically dependent on prevailing winds. Although we considered the possibility of using predominant winds together with distance to refine the definition of industrial proximity, winds in Asturias display a pronounced seasonal nature, as is reflected by the wind roses depicted in Fig. 1, which renders it difficult to define prevailing winds in the study area.

Inevitably, the use of hospital-based controls is a potential limitation. In this particular instance, the hospitals where the cases were recruited were referral centers for all patients requiring hospitalization. Our controls had been referred to these hospitals owing to the presence of acute health conditions thought to be unrelated to the main lung cancer risk factors. The geographic distribution of the control population likely reflects population density in the health areas studied. Although there is always a chance of recall bias being present, the fact that information on confounding variables was obtained retrospectively means that the risk estimators obtained for well-known risk factors, such as tobacco exposure and occupation, were in line with the literature.

Our results show that the excess risks associated with industrial pollution were concentrated in the vicinity of metal industries (principally, metal galvanizing and surface-treatment installations), cement plants and shipyards. Emissions from these industries include: recognized carcinogens in humans, such as arsenic and inorganic arsenic compounds, benzene, cadmium, nickel compounds, chromium, dioxins, asbestos, formaldehyde, radon, silica, crystalline, soot, coal-tar pitches, and some polycyclic aromatic hydrocarbons (PAHs); probable carcinogens, such as tetrachloroethylene, trichloroethylene, acrylamide, and nitrosamines; or possible carcinogens, such as lead, nickel, furans, ethylbenzene, hexachloroethane, and welding fumes (IARC 2012; Tossavainen 1990).

Residence in the vicinity of metal industries located in our study area showed a statistically significant excess risk of lung cancer when they were studied as a whole. We attempted to investigate specific excess risks by type of industrial activity within this broad class of industry. The metal sector includes installations for steel founding and aluminum production, two industrial activities classified by

Table 2 Odds ratios of lung cancer associated with residential proximity to industrial facilities, by distance

Distance (km)	Exposure category	Controls *N*	Cases *N*	OR (95 % CI)[a]
5				
	Reference	121	94	–
	All industries (only)	509	525	1.18 (0.82–1.69)
	Intersection with urban area[b]	70	81	1.41 (0.86–2.31)
4				
	Reference	139	106	–
	All industries (only)	491	513	1.28 (0.91–1.80)
	Intersection with urban area[b]	70	81	1.50 (0.92–2.43)
3				
	Reference	247	187	–
	All industries (only)	383	432	**1.43 (1.08–1.89)**
	Intersection with urban area[b]	70	81	**1.55 (1.00–2.40)**
2.5				
	Reference	320	278	–
	All industries (only)	310	341	1.21 (0.93–1.59)
	Intersection with urban area[b]	70	81	1.36 (0.89–2.06)
2				
	Reference	395	360	–
	All industries (only)	235	259	1.13 (0.87–1.48)
	Intersection with urban area[b]	70	81	1.29 (0.86–1.95)

Bold values indicate significant results and different sectors

[a] ORs were estimated from a multiple logistic regression model that included age, sex, hospital area, tobacco consumption, family history of cancer, area of residence, and occupation

[b] Intersection area between industrial area corresponding to each industrial sector and urban area

Table 3 Odds ratios of lung cancer by industrial sector

Industrial sector (no. industries)	Individuals residing ≤3 km		
	Controls *N*	Cases *N*	OR (95 % CI)[a]
Reference	247	187	
All industries (48)	383	187	**1.43 (1.08–1.89)**
Intersection with urban area[b]	70	81	**1.55 (1.00–2.40)**
Energy sector (4)	9	13	1.68 (0.62–4.56)
Metal industry (15)	330	375	**1.40 (1.05–1.87)**
Intersection with urban area[b]	64	76	**1.57 (1.00–2.46)**
Steel production and founding (2)	39	51	1.27 (0.73–2.21)
Intersection with urban area[b]	5	5	0.93 (0.20–4.37)
Galvanizing (4)	245	282	**1.66 (1.18–2.33)**
Intersection with urban area[b]	44	64	**2.14 (1.27–3.61)**
Iron founding (1)	3	2	0.97 (0.12–7.82)
Non-ferrous metal smelters (5)	29	25	0.81 (0.41–1.63)
Intersection with urban area[b]	17	12	0.87 (0.35–2.15)
Surface treatment (3)	179	193	1.32 (0.93–1.89)
Intersection with urban area[b]	3	0	0 (0–inf)
Mineral industry (14)	97	100	1.32 (0.87–2.01)
Intersection with urban area[b]	26	17	0.86 (0.40–1.82)
Mining (3)	8	6	0.62 (0.16–2.45)
Production of cement (3)	4	9	**4.81 (1.20–19.19)**
Production of glass and ceramic (8)	88	91	1.31 (0.85–2.02)
Intersection with urban area[b]	26	17	0.85 (0.40–1.81)
Chemical industry (5)	34	41	1.38 (0.76–2.51)
Waste management (4)	8	10	1.18 (0.39–3.53)
Food and beverage sector (4)	16	14	1.08 (0.40–2.93)
Shipyards (1)	234	260	**1.69 (1.17–2.43)**
Intersection with urban area[b]	39	59	**2.37 (1.36–4.15)**
Textile industry (1)	7	8	1.15 (0.36–3.73)

Bold values indicate significant results and different sectors

[a] ORs were estimated from a multiple logistic regression model that included age, sex, hospital area, tobacco consumption, family history of cancer, area of residence, and occupation

[b] Intersection area between industrial area corresponding to each industrial sector and urban area

the IARC as implying a carcinogenic risk to humans (IARC 2012), and reported by some occupational and/or environmental studies as being associated with lung cancer (Benedetti et al. 2001; Bosetti et al. 2007; Gibbs et al. 2007; Pershagen and Simonato 1990; Rodriguez et al. 2000; Spinelli et al. 2006). Nevertheless, our results—with few exceptions—failed to show any consistent excess risk around such industrial activities. One of the most interesting results of our study was the high excess risk of lung cancer found among subjects living close to galvanizing installations. The galvanizing sector is one of the industrial activities that releases dioxins to air (ATEG-Grupo Interlab 2005) and is included in the Spanish National Dioxin and Furane Inventory (Martinez et al. 2008). Dioxins are recognized by the IARC as carcinogens in humans (IARC 2012), and there are studies that have observed increased risks for all cancers combined, and for lung cancer in particular (IARC 1997). In our analysis by type of pollutant released, we found a high, though non-statistically significant, excess risk for dioxins. Another interesting result was the almost statistically significant excess risk found in the proximity of electrolytic or chemical surface-treatment installations. As in the case of galvanizing installations, these types of metal industries use metalworking fluids (MWFs), a range of oils and other chemical substances used to cool and/or lubricate metal workpieces when they are being machined, ground, milled, etc., and known to be carcinogens in humans (Savitz 2003). Some occupational studies have found excess of lung cancer mortality among workers exposed to certain types of MWFs and mineral oils (Acquavella et al. 1993; DHHS (NIOSH) 1998; Kazerouni et al. 2000; Tolbert 1997). Furthermore, one study detected a slightly increased lung cancer mortality rate in United

Table 4 Odds ratios of lung cancer by facility

Facility[a] (PRTR code)	Individuals residing ≤3 km Controls N	Cases N	OR (95 % CI)[b]
Reference	247	187	
Energy sector			
2928	6	9	1.62 (0.49–5.32)
Metal industry			
Steel production and founding			
3486	27	39	1.42 (0.76–2.68)
6827	12	12	0.80 (0.25–2.55)
6827 + urban area[c]	5	5	0.83 (0.17–3.99)
Galvanizing			
1850	11	13	0.96 (0.30–3.05)
1850 + urban area[c]	5	5	0.87 (0.18–4.15)
1925	6	10	1.60 (0.51–5.05)
1948	50	60	**1.74 (1.04–2.90)**
3096	227	258	**1.79 (1.24–2.59)**
3096 + urban area[c]	39	59	**2.45 (1.40–4.28)**
Non-ferrous metal smelters			
1477	11	14	1.30 (0.48–3.49)
1477 + urban area[c]	7	6	1.03 (0.29–3.66)
1937	3	3	0.62 (0.11–3.39)
3512	4	2	0.56 (0.07–4.24)
3551	21	19	0.86 (0.39–1.93)
3551 + urban area[c]	17	12	0.88 (0.36–2.17)
Surface treatment			
1554	29	35	1.44 (0.61–3.41)
3545	147	156	1.32 (0.91–1.92)
6546	4	2	0.56 (0.07–4.24)
Mineral industry			
Mining			
6592	5	5	0.83 (0.17–3.92)
Production of cement			
1915	3	6	2.80 (0.57–13.71)
Production of glass and ceramic			
1929	32	29	1.05 (0.54–2.06)
1929 + Urban area[c]	23	17	0.95 (0.43–2.09)
1934	25	26	1.23 (0.52–2.93)
3888	4	2	0.56 (0.07–4.24)
4551	5	2	0.44 (0.07–2.95)
6179	23	31	1.78 (0.91–3.48)
Chemical industry			
1582	10	15	1.54 (0.60–3.95)
1936	6	2	0.43 (0.07–2.81)
3550	17	23	1.57 (0.72–3.45)
Waste management			
1928	5	9	1.38 (0.40–4.84)
Food and beverage sector			
748	13	10	0.90 (0.30–2.74)
Shipyards			
6511	234	260	**1.69 (1.17–2.43)**
6511 + urban area[c]	39	59	**2.37 (1.36–4.15)**
Textile industry			
3566	7	8	1.15 (0.36–3.73)

Bold values indicate significant results and different sectors

[a] Facilities with number of cases + controls >5 and number of cases >0

[b] ORs were estimated from a multiple logistic regression model that included age, sex, hospital area, tobacco consumption, family history of cancer, area of residence, and occupation

[c] Intersection area between industrial area corresponding to each facility and urban area

Table 5 Odds ratios of lung cancer by carcinogens released or type of industry

Exposure type	Individuals residing ≤3 km Controls N	Cases N	OR (95 % CI)[a]
Carcinogens[b]			
Arsenic–cadmium–chromium	144	155	0.76 (0.37–1.59)
Nickel	189	207	1.21 (0.72–2.03)
Dioxins + furans	47	67	1.59 (0.84–3.01)
Carcinogenic industry[b]			
Shipyards	273	319	**1.69 (1.17–2.45)**
Aluminum production	20	20	0.81 (0.36–1.84)
Iron and steel founding	20	19	0.54 (0.20–1.47)
Other IPPC industries	37	45	1.38 (0.79–2.40)

Bold values indicate significant results and different sectors

[a] ORs were estimated from a multiple logistic regression model that included age, sex, hospital area, tobacco consumption, family history of cancer, area of residence, and occupation

[b] This table includes carcinogens and type of industries classified by the IARC as a group 1 carcinogen

States counties with metal electroplating industries (Blair and Mason 1980). Lastly, it should be noted that, as reported in a previous paper (Garcia-Perez et al. 2010), the primary metal industry is a major environmental contributor of chlorinated solvents. According to the European Chlorinated Solvent Association (ECSA), chlorinated solvents are defined as methylene chloride (dichloromethane), perchloroethylene (tetrachloroethylene) and trichloroethylene (Chlorine Online 2013), and are mainly used in dry-cleaning, machine cleaning, metal degreasing and surface treatment. Both tetrachloroethylene and trichloroethylene

Table 6 Types of carcinogenic substances and amounts released to air by facility, in kg/year (PRTR-Spain, 2007)

Facility (PRTR code)	Arsenic	Cadmium	Chromium	Nickel	Dioxins + furans
Energy sector	184	108	770	725	2.0E−05
1594	0	0	0	0	0
1942	2	4	9	30	0
2927	69	104	70	114	2.0E−05
2928	113	0	691	581	0
Metal industry	67	128	223	234	3.4E−03
Steel production and founding	66	128	222	231	3.4E−03
1923	0	0	0	0	0
3486	66	128	222	231	3.4E−03
6827	0	0	0	0	0
Galvanizing	0.1	0.02	0.1	2.1	6.1E−07
1850	0.1	0.02	0.1	0.1	6.1E−07
1925	0	0	0	0	0
1948	0	0	0	2	0
3096	0	0	0	0	0
Non-ferrous metal smelters	0.6	0.3	0.3	0.3	0
1477	0	0	0	0	0
1937	0	0	0	0	0
1943	0.6	0.3	0.3	0.3	0
3512	0	0	0	0	0
3551	0	0	0	0	0
Surface treatment	0	0	0.5	0.8	0
1554	0	0	0.4	0.7	0
3545	0	0	0	0	0
6546	0	0	0.04	0.1	0
Mineral industry	50	46	88	220	3.4E−05
Mining	0	0	0	0	0
6590	0	0	0	0	0
6591	0	0	0	0	0
6592	0	0	0	0	0
Production of cement	36	43	35	105	3.4E−05
1914	8	4	20	44	1.0E−05
1915	20	7	11	24	2.4E−05
1944	8	32	5	37	0
Production of glass and ceramic	15	3	53	115	0
1920	0	0	0	0	0
1922	0	0	0	0	0
1929	6	2	48	110	0
1934	0.9	0.4	1	2	0
3888	7	0.1	1	0	0
4551	0	0	0	0	0
5483	1	0.7	2	3	0
6179	0	0	0	0	0
Chemical industry	0	0	0	0	5.3E−06
1582	0	0	0	0	0
1918	0	0	0	0	5.3E−06
1936	0	0	0	0	0
3550	0	0	0	0	0
6653	0	0	0	0	0

Table 6 continued

Facility (PRTR code)	Arsenic	Cadmium	Chromium	Nickel	Dioxins + furans
Waste management	0.2	0.1	0.5	10	0
1928	0	0	0	0	0
1935	0.2	0.1	0.5	10	0
1938	0	0	0	0	0
3905	0	0	0	0	0
Food and beverage sector	0.004	0.02	0	0.04	0
51	0	0	0	0	0
748	0	0	0	0	0
1924	0	0	0	0	0
5821	0.004	0.02	0	0.04	0
Shipyards	0	0	0	0	0
6511	0	0	0	0	0
Textile industry	0	0	0	0	0
3566	0	0	0	0	0

are recognized as probable carcinogens according to the IARC (IARC 2012), and one study found an elevated risk for lung adenocarcinoma in men exposed to trichloroethylene (Siemiatycki 1991). Moreover, animal experiments have shown that tetrachloroethylene and trichloroethylene cause lung carcinoma in mice (IARC 1995). It should be stressed that chlorinated solvents are released into the environment, chiefly as toxic waste discharged into water drainage areas by the metal sector, and that on the whole, effluents from metal industries are genotoxic, in that they induce cytogenetic damage, mutations, and DNA damage in repair processes (Claxton et al. 1998; Houk 1992).

Insofar as cement plants are concerned, they release several carcinogenic substances recognized by the IARC, such as arsenic, cadmium, chromium, dioxins or asbestos (IARC 2012) (see Table 6). In this regard, Fano observed a significant excess risk of lung cancer among people living in the proximity of a cement plant (Fano et al. 2004), an ecologic study conducted in Lithuania documented excess risk of lung cancer among male cement workers (Smailyte et al. 2004), and a recent IARC multicenter case–control study on occupation reported an elevated lung cancer risk among men involved in the cement industry (Bardin-Mikolajczak et al. 2007). In addition, a meta-analysis revealed an association between occupational exposure to asbestos in cement workers and lung cancer (Goodman et al. 1999).

Finally, the shipyard included in our study, situated in Gijon and around which we detected a high, statistically significant increased risk of lung cancer, was founded in 1911 and, therefore, those subjects residing close to this facility have been exposed to its emissions during a long period of time. Shipyards are well-known emitters of asbestos (Beckett 2007; Hollins et al. 2009; Tomioka et al. 2011), a substance recognized by the IARC as a lung carcinogen in humans (IARC 2012). In this connection, Barbone et al. found an excess risk of lung adenocarcinoma in the proximity of a shipyard in Trieste, Italy (Barbone et al. 1995), and Bianchi et al. stated that asbestos exposure may reach alarming levels in shipyard areas (Bianchi et al. 2000). In addition, some occupational studies have reported excess lung cancer mortality in such installations (Jeong et al. 2011; Krstev et al. 2007; Seel et al. 2007).

This paper analyzed lung cancer risk by type of industry and carcinogens released. This information was solely available for recent years, and it thus follows that current exposure may not be an appropriate surrogate of the exposure situation 10 years prior to diagnosis of the study participants. Bearing this in mind, however, it is interesting to note that high, though non-statistically significant, excess risks were found for residents living close to industrial facilities which released dioxins and nickel. As previously mentioned, dioxins are recognized by the IARC as carcinogens in humans (IARC 2012) and there are studies that have observed increased risks for lung cancer (IARC 1997). Likewise, there are some studies reporting increased risk of lung cancer among workers exposed to nickel, e.g., lung cancer mortality was observed to be modestly increased among workers at a nickel carbonyl refinery (Sorahan and Williams 2005), and specifically, among those employees who had spent at least 5 years working in the feed-handling and nickel extraction departments. This increased lung cancer risk was confirmed in a separate analysis of the same nickel refinery cohort, using combined data from two separate studies (Grimsrud and Peto 2006).

Conclusion

In conclusion, our study furnishes further evidence that living in the proximity (≤3 km) of certain industrial installations is a risk factor for lung cancer. Specifically, residents living near metal industries (principally, galvanizing installations), cement plants and shipyards showed an increased risk. In addition, analysis by carcinogenic substance or activity showed a non-statistically significant excess risk of lung cancer in the proximity of installations releasing dioxins–furans and nickel.

Acknowledgments We are indebted to all the patients who participated in the study. We should also like to thank our technical colleagues (Molecular Epidemiology of Cancer Unit, University Institute of Oncology of the Principality of Asturias/*Instituto Universitario de Oncología del Principado de Asturias*) for collecting the data, and our statistician, Ana Fernández-Somoano, for her valuable contribution. This study was funded by Spain's Health Research Fund (Fondo de Investigación Sanitaria—grants FIS CD07/00283 and FIS-07-BI060604).

Conflict of interest The authors declare that they have no conflict of interests.

References

Acquavella J, Leet T, Johnson G (1993) Occupational experience and mortality among a cohort of metal components manufacturing workers. Epidemiology 4:428–434

Área de Epidemiología Ambiental y cáncer—Centro Nacional de Epidemiología—ISCIII (2013) Mortalidad por cáncer y otras causas en España. Año 2008. Available at: http://www.isciii.es/ISCIII/es/contenidos/fd-servicios-cientifico-tecnicos/fd-vigilancias-alertas/fd-epidemiologia-ambiental-y-cancer/mortal2008.pdf

Armenian HK, Lilienfeld AM (1974) The distribution of incubation periods of neoplastic diseases. Am J Epidemiol 99:92–100

ATEG-Grupo Interlab (2005) Documento de orientación sectorial para la medición, cálculo y estimación de emisiones de sustancias EPER. Available at: http://www.prtr-es.es/data/images/Documento%20de%20Orientaci%C3%B3n%20sectorial%20para%20la%20Medici%C3%B3n,%20c%C3%A1lculo%20o%20estimaci%C3%B3n%20en%20el%20sector%20de%20Galvanizaci%C3%B3n-B58165BF51317168.pdf

Barbone F, Bovenzi M, Cavallieri F, Stanta G (1995) Air pollution and lung cancer in Trieste, Italy. Am J Epidemiol 141:1161–1169

Bardin-Mikolajczak A, Lissowska J, Zaridze D, Szeszenia-Dabrowska N, Rudnai P, Fabianova E, Mates D, Navratilova M, Bencko V, Janout V, Fevotte J, Fletcher T, Mannetje TA, Brennan P, Boffetta P (2007) Occupation and risk of lung cancer in Central and Eastern Europe: the IARC multi-center case–control study. Cancer Causes Control 18:645–654

Batchgeo (2013). Available at: http://www.batchgeo.com/en/

Beckett WS (2007) Shipyard workers and asbestos: a persistent and international problem. Occup Environ Med 64:639–641

Belli S, Benedetti M, Comba P, Lagravinese D, Martucci V, Martuzzi M, Morleo D, Trinca S, Viviano G (2004) Case–control study on cancer risk associated to residence in the neighbourhood of a petrochemical plant. Eur J Epidemiol 19:49–54

Benedetti M, Iavarone I, Comba P (2001) Cancer risk associated with residential proximity to industrial sites: a review. Arch Environ Health 56:342–349

Bianchi C, Brollo A, Ramani L (2000) Asbestos exposure in a shipyard area, northeastern Italy. Ind Health 38:301–308

Blair A, Mason TJ (1980) Cancer mortality in United States counties with metal electroplating industries. Arch Environ Health 35:92–94

Bosetti C, Boffetta P, La Vecchia C (2007) Occupational exposures to polycyclic aromatic hydrocarbons, and respiratory and urinary tract cancers: a quantitative review to 2005. Ann Oncol 18: 431–446

Catelinois O, Rogel A, Laurier D, Billon S, Hemon D, Verger P, Tirmarche M (2006) Lung cancer attributable to indoor radon exposure in france: impact of the risk models and uncertainty analysis. Environ Health Perspect 114:1361–1366

Chlorine Online (2013) About chlorinated solvents. Available at: http://www.eurochlor.org/chlorinated-solvents-%28ecsa%29/about-chlorinated-solvents.aspx

Clapp RW, Howe GK, Jacobs MM (2005) Environmental and occupational causes of cancer. A review of recent Scientific Literature. Lowell Center for Sustainable Production, Lowell

Claxton LD, Houk VS, Hughes TJ (1998) Genotoxicity of industrial wastes and effluents. Mutat Res 410:237–243

DHHS (NIOSH) (1998) Criteria for a recommended standard: occupational exposure to metalworking fluids. No. 98-102, National Institute for Occupational Safety and Health

European Commission Environment (2012) The IPPC Directive. Available at: http://ec.europa.eu/environment/air/pollutants/stationary/ippc/index.htm

Fano V, Michelozzi P, Ancona C, Capon A, Forastiere F, Perucci CA (2004) Occupational and environmental exposures and lung cancer in an industrialised area in Italy. Occup Environ Med 61:757–763

Ferlay J, Shin HR, Bray F, Forman D, Mathers C, Parkin DM (2010) Estimates of worldwide burden of cancer in 2008: GLOBOCAN 2008. Int J Cancer 127:2893–2917

Fernandez-Rubio A, Lopez-Cima MF, Gonzalez-Arriaga P, Garcia-Castro L, Pascual T, Marron MG, Tardon A (2008) The TP53 Arg72Pro polymorphism and lung cancer risk in a population of Northern Spain. Lung Cancer 61:309–316

Garcia-Perez J, Boldo E, Ramis R, Vidal E, Aragones N, Perez-Gomez B, Pollan M, Lopez-Abente G (2008) Validation of the geographic position of EPER-Spain industries. Int J Health Geogr. 7:1

Garcia-Perez J, Pollan M, Boldo E, Perez-Gomez B, Aragones N, Lope V, Ramis R, Vidal E, Lopez-Abente G (2009) Mortality due to lung, laryngeal and bladder cancer in towns lying in the vicinity of combustion installations. Sci Total Environ 407:2593–2602

Garcia-Perez J, Lopez-Cima MF, Boldo E, Fernandez-Navarro P, Aragones N, Pollan M, Perez-Gomez B, Lopez-Abente G (2010) Leukemia-related mortality in towns lying in the vicinity of metal production and processing installations. Environ Int 36:746–753

Gibbs GW, Armstrong B, Sevigny M (2007) Mortality and cancer experience of Quebec aluminum reduction plant workers. Part 2: mortality of three cohorts hired on or before January 1, 1951. J Occup Environ Med 49:1105–1123

Gonzalez CA, Riboli E (2010) Diet and cancer prevention: contributions from the European Prospective Investigation into Cancer and Nutrition (EPIC) study. Eur J Cancer 46:2555–2562

Gonzalez-Arriaga P, Lopez-Cima MF, Fernandez-Somoano A, Pascual T, Marron MG, Puente XS, Tardon A (2008) Polymorphism +17 C/G in matrix metalloprotease MMP8 decreases lung cancer risk. BMC Cancer 8:378

Goodman M, Morgan RW, Ray R, Malloy CD, Zhao K (1999) Cancer in asbestos-exposed occupational cohorts: a meta-analysis. Cancer Causes Control 10:453–465

Grimsrud TK, Peto J (2006) Persisting risk of nickel related lung cancer and nasal cancer among Clydach refiners. Occup Environ Med 63:365–366

Hollins DM, Paustenbach DJ, Clark K, Mangold CA (2009) A visual historical review of exposure to asbestos at puget sound naval shipyard (1962–1972). J Toxicol Environ Health B Crit Rev 12:124–156

Houk VS (1992) The genotoxicity of industrial wastes and effluents. Mutat Res 277:91–138

IARC (1986) Monographs on the evaluation of carcinogenic risks to humans, vol 38. Tobacco smoking. Available at: http://www.iarc.fr/en/publications/list/monographs/

IARC (1995) Monographs on the evaluation of carcinogenic risks to humans, vol 63. Dry-Cleaning, some chlorinated solvents and other industrial chemicals. Available at: http://monographs.iarc.fr/ENG/Monographs/vol63/index.php

IARC (1997) Monographs on the evaluation of carcinogenic risks to humans, vol 69. Polychlorinated Dibenzo-*para*-dioxins and Polychlorinated Dibenzofurans. Available at: http://monographs.iarc.fr/ENG/Monographs/vol69/index.php

IARC (2012) Monographs on the evaluation of carcinogenic risks to humans. Available at: http://monographs.iarc.fr/ENG/Classification/ClassificationsGroupOrder.pdf

Jeong KS, Kim Y, Kim MC, Yoo CI (2011) Comparison of cancer incidence between production and office workers at a shipyard in Korea: A retrospective cohort study from 1992 to 2005. Am J Ind, Med

Kazerouni N, Thomas TL, Petralia SA, Hayes RB (2000) Mortality among workers exposed to cutting oil mist: update of previous reports. Am J Ind Med 38:410–416

Krstev S, Stewart P, Rusiecki J, Blair A (2007) Mortality among shipyard Coast Guard workers: a retrospective cohort study. Occup Environ Med 64:651–658

Leader A, Fernandez-Somoano A, Lopez-Cima MF, Gonzalez-Arriaga P, Pascual T, Marron MG, Tardon A (2010) Educational inequalities in quantity, duration and type of tobacco consumption among lung cancer patients in Asturias: epidemiological analyses. Psicothema 22:634–640

Lopez-Cima MF, Gonzalez-Arriaga P, Garcia-Castro L, Pascual T, Marron MG, Puente XS, Tardon A (2007) Polymorphisms in XPC, XPD, XRCC1, and XRCC3 DNA repair genes and lung cancer risk in a population of northern Spain. BMC Cancer. 7:162

Lopez-Cima MF, Garcia-Perez J, Perez-Gomez B, Aragones N, Lopez-Abente G, Tardon A, Pollan M (2011) Lung cancer risk and pollution in an industrial region of Northern Spain: a hospital-based case–control study. Int J Health Geogr 10:10

Marin MS, Lopez-Cima MF, Garcia-Castro L, Pascual T, Marron MG, Tardon A (2004) Poly (AT) polymorphism in intron 11 of the XPC DNA repair gene enhances the risk of lung cancer. Cancer Epidemiol Biomarkers Prev 13:1788–1793

Martinez MA, Sanz P, Ruiz ML, Fabrellas B, Abad E, Rivera J (2008) Evaluation of the Spanish hot dip galvanising sector as a source of polychlorinated dibenzo-*p*-dioxins and polychlorinated dibenzofurans. Chemosphere 71:1127–1134

Ministerio de Medio Ambiente y Medio Rural y Marino (2011) Sistema de Información Geográfica de Parcelas Agrícolas (SIGPAC). Available at: http://www.marm.es/es/agricultura/temas/sistema-de-informacion-geografica-de-parcelas-agricolas-sigpac-/

Office of Federal Statistical Policy and Standards (1972) Standard industrial classification manual. US Government Printing Office, Washington, DC

Office of Federal Statistical Policy and Standards (1977) Standard occupational classification manual. US Government Printing Office, Washington, DC

Parodi S, Stagnaro E, Casella C, Puppo A, Daminelli E, Fontana V, Valerio F, Vercelli M (2005) Lung cancer in an urban area in Northern Italy near a coke oven plant. Lung.Cancer 47:155–164

Pershagen G, Simonato L (1990) Epidemiological evidence for the carcinogenity of air pollutants. Air pollutant and human cancer. In: Tomatis L (ed) European School of Oncology monograph. Springer-Verlag, Berlin

Pizzo AM, Chellini E, Costantini AS (2011) Lung cancer risk and residence in the neighborhood of a sewage plant in Italy. A case–control study. Tumori 97:9–13

Pless-Mulloli T, Phillimore P, Moffatt S, Bhopal R, Foy C, Dunn C, Tate J (1998) Lung cancer, proximity to industry, and poverty in northeast England. Environ Health Perspect 106:189–196

Raaschou-Nielsen O, Andersen Z, Hvidberg M, Jensen S S, Ketzel M, Sorensen M, Loft S, Overvad K, Tjonneland A (2011) Lung Cancer incidence and long-term exposure to air pollution from traffic. Environ Health Perspect 119(6):860–865

Rodriguez V, Tardon A, Kogevinas M, Prieto CS, Cueto A, Garcia M, Menendez IA, Zaplana J (2000) Lung cancer risk in iron and steel foundry workers: a nested case control study in Asturias, Spain. Am J Ind Med 38:644–650

Savitz DA (2003) Epidemiologic evidence on the carcinogenicity of metalworking fluids. Appl Occup Environ Hyg 18:913–920

Seel EA, Zaebst DD, Hein MJ, Liu J, Nowlin SJ, Chen P (2007) Inter-rater agreement for a retrospective exposure assessment of asbestos, chromium, nickel, and welding fumes in a study of lung cancer and ionizing radiation. Ann Occup Hyg 51:601–610

Siemiatycki J (1991) Risk factors for cancer in the workplace. CRC Press, Boca Raton

Smailyte G, Kurtinaitis J, Andersen A (2004) Mortality and cancer incidence among Lithuanian cement producing workers. Occup Environ Med 61:529–534

Smith GH, Williams FL, Lloyd OL (1987) Respiratory cancer and air pollution from iron foundries in a Scottish town: an epidemiological and environmental study. Br J Ind Med 44:795–802

Sociedad asturiana de estudios económicos e industriales (sadei) (2011) Nomenclátor de entidades de población 2010. Available at: http://www.sadei.es/

Sorahan T, Williams SP (2005) Mortality of workers at a nickel carbonyl refinery, 1958–2000. Occup Environ Med 62:80–85

Spinelli JJ, Demers PA, Le ND, Friesen MD, Lorenzi MF, Fang R, Gallagher RP (2006) Cancer risk in aluminum reduction plant workers (Canada). Cancer Causes Control 17:939–948

Tolbert PE (1997) Oils and cancer. Cancer Causes Control 8:386–405

Tomioka K, Natori Y, Kumagai S, Kurumatani N (2011) An updated historical cohort mortality study of workers exposed to asbestos in a refitting shipyard, 1947–2007. Int Arch Occup Environ Health 84:959–967

Tossavainen A (1990) Estimated risk of cancer attributable to occupational exposures in iron and steel foundries. In: Vainio H, Sorsa M, McMichael AJ (eds) Complex mixtures and cancer risk. IARC Scientific Publications, Lyon, pp 363–367