

Occupational exposure and lung cancer in Italy: estimating the number of workers potentially at risk

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Abstract. *Background:* In 2001, a comprehensive and standardised list for occupations or jobs known or suspected to be associated with lung cancer was prepared. The aim of this study was to assess the number of potentially exposed workers using this list. *Methods:* A detailed and unique list of codes has been developed on the basis of the national standard classification of economic activities. The list is divided into two categories: one of occupations definitely entailing carcinogenic risk and another of those which probably/possibly entail a risk. Firms have been selected from ISPESL database of enterprises and the number of workers has been estimated on the basis of this list. *Results:* The number of potentially exposed workers in “industry and services” sector, related to lung cancer risk, is 650,886 blue-collar workers and the number of firms censused in Italy is 117,006 units. These figures – based on administrative sources rather than on direct measures of exposure – are likely to overestimate potential exposure to carcinogenic agents. *Conclusions:* The list founded on a standard classification permits the creation of databases to control occupational exposure to carcinogens and to increase comparability between epidemiologic studies based on job-exposure matrices. (www.actabiomedica.it)

Key words: Lung cancer, occupational exposure, Italy, risk

Introduction

Occupational exposure is a well-known risk factor for lung cancer (1-2). The first associations between lung cancer and working activity were found for nickel, cobalt, arsenic and uranium miners during the first decades of the Twentieth Century, but they can be traced back to the Sixteenth Century (3-6).

Since the risk is connected with industrial activity and working profession, it is extremely important to draw up lists of occupations considered or suspected to be associated with lung cancer. The first lists were published in 1982 on the basis of IARC (International Agency for Research on Cancer) monographs, and are divided into two groups: list A contains the activities proved to be carcinogenic to man; list B contains

the activities probably carcinogenic to man. In the following years, the lists have been updated and improved (7-8).

An interesting study has been made in Germany to evaluate occupationally related lung cancer in the northern regions (9). All Germans with a carcinoma of the lung diagnosed no more than 3 months at the date of the research, have been interviewed and classified according to the lists of occupations A and B. As a result, one quarter of the recent diagnosed cases have a professional origin. It is possible to compare these lists to the list of Sentinel Health Events (Occupational) prepared by Rutstein to match 50 occupational diseases, among which lung cancer, to their proved or suspected causing occupations and industries (10). Differently from lists A and B, Rutstein's list included hazardous agents. Moreover, lung cancer has been in-

serted in the sub list of diseases which may or may not be related to occupation.

There are various classifications of occupations and industrial activities, such as the International Standard Classification of Occupations (ISCO) and the International Standard Industrial Classification of all Economic Activities (ISIC), developed in 1958 by the International Labour Office, which are the base for current NACE classification, the Statistical Classification of Economic Activities in the European Community. In the US the main classifications of occupations are the Bureau of Census classification, the Dictionary of Occupational Titles (DOT), and the Standard Occupational Classification (SOC) developed in 1966. While concerning industries, US developed in 1930 the Standard Industrial Classification (SIC), replaced by the North American Industry Classification System (NAISC) in 1997 (11). Many countries, like Russia, Japan, Mexico, Brazil have developed their own lists of occupations and industries. Russian studies related to the lists have shown that workers at high risk belong to manufacturing, chemistry and metal production sectors (12). Differently, the British Registrar General's Scale (11) takes into consideration also the skill level of workers, classified in five categories (I professional; II managerial and technical; III skilled non-manual; IIIM skilled manual; IV partly skilled; V unskilled). Moreover, Ahrens et al. have proposed a list (A) of occupations and industries associated with lung cancer and a list (B) of occupations and industries probably related to the disease. The lists are based on ISCO 68 and ISIC Rev. 2 (13).

In Italy, the Unit of Cancer Epidemiology, Center for Cancer Epidemiology and Prevention of Piedmont (CPO) in cooperation with the National Institute for Occupational Prevention and Safety (ISPESL) listed, in 2001, the codified activities in a uniformed and standardized way, for univocal and coherent evaluation of professional exposure in epidemiologic studies (14). Differently from other lists or matrices of occupational exposure based on carcinogenic substances used for a specific job, this list has been prepared in reference to industrial activities or occupations linked to a high lung cancer mortality rate, as documented in scientific literature. Such a list could be a valid instrument to es-

timate the risk of occupational exposure in epidemiological studies.

Objective

This study is part of a wider research project "Strategies and innovative indicators for the assessment of gene-environment interactions in occupational lung cancers" supported in 2003 by the Italian Ministry of Health, and some results have already been published (15). In this paper, data about the geographical distribution of workers potentially exposed to carcinogenic agents associated with lung cancer risk are reported in detail. The estimate refers to the lists of industrial activities considered or suspected to be related to lung cancer risk, and is based on ISPESL database of enterprises operating in Italy.

Methods

The selection procedure for activity sector codes is extensively described elsewhere (15). Briefly, Ateco91 ISTAT (National Institute of Statistics) codes have been selected starting from lists A and B of industrial activities and occupations known or suspected to be related to lung cancer, elaborated by CPO. Ateco91 is the national classification of economic activities and is based on NACE Revision 1 codes, the official classification of economic activities in the European Union (16).

Every activity or job present in lists A and B has been coded in the most analytical way. When it has not been possible to determine a detailed code for an industrial process, a more generic Ateco91 code has been selected. During the generalization of codes, an item could appear in both lists A and B. In this case, the code has been attributed to the list where it appears more frequently (e.g. code 24.24 has been considered only in list B because it is related to industrial processes and jobs listed more in group B than in A). If both lists presented the same conditions for an item, the code has been attributed to list A which is the most relevant. These circumstances have happened very rarely. A complete description of tables A and B,

as well as their codification, is available on the Institute's website (17).

After selecting and distributing Ateco91 codes to both groups, a list of companies and their number of workers has been extracted from ISPEL enterprises archive, updated on December 31, 1998. ISPEL database design is fully described elsewhere (18). In brief, it is a nominal archive of companies prepared with a matching procedure on the basis of the Fiscal Code or VAT Number of companies present in the National Chamber of Commerce (UNIONCAMERE) and the National Social Security Institute (INPS) archives. The database is organized on different levels of reliability of matching data accuracy (companies matched or not) and occupational levels present in both sources (correspondence of total number of workers).

In this study, the companies present in both INPS and UNIONCAMERE archives have been selected, this means to consider the first three levels of reliability out of the available six. In correspondence to the first three levels of reliability, the number of workers is certain (available and corresponding in both archives) or reassessed through an algorithm which considers ISTAT data (19) on Italian workers in 1991 (in case of no correspondence of the two archives). To calculate the number of exposed workers, blue-collars and white-collars have been considered separately on the basis of INPS classification. INPS archives do not contain data belonging to State railways, agriculture and State administration companies. Thus, these sectors have not been considered here.

In order to evaluate the correlation between exposed workers and lung cancer deaths, the rate between exposed workers and per 100,000 resident population (T_{exp}), and the rate between deaths and per 100,000 resident population (T_{dth}) for each $i_{i,b}$ province have been estimated. The resident population was taken from the last population census (ISTAT, 2001) and the number of lung cancer deaths from 2001 ISTAT mortality data statistics. After having verified the statistical significance of such correlation, it has been performed a linear regression analysis. The linear model was: $T_{dth}_i = \alpha + \beta T_{exp}_i + \varepsilon_i$, for $i=1$ to 103 (Italian provinces). The statistical significance of estimated regression coefficients (α , β) and the

goodness of fit (r-squared) between empirical and predicted values were also evaluated.

Results

According to the list described in Methods section, 117,006 companies and 650,886 workers have been selected from ISPEL registry concerning the sector "industry and services". The division between proven and probable activities at risk is the following: 33,232 companies and 210,465 workers (blue-collars) classified in list A, and 83,774 companies with 440,421 workers in list B. White-collars are 112,926 in list A and 224,880 in list B.

Table 1 shows the distribution of companies belonging to list A and B, according to the economic activity (for *section* and *subsection* of activity) in industry and services sector. The distribution of workers (blue-collars) at risk of lung cancer by Italian geographical areas is shown in Figure 1.

In the North-West (NW) area of Italy the highest number of exposed workers in list A results for "28.75-Manufacture of other fabricated metal products n.e.c." (20,278 blue-collars), followed by "28.51-Treatment and coating of metals" (12,934) and "45.23-Construction of highways, roads, airfields and sport facilities" (5,135), whereas in the Nord-East (NE) area the highest values result for "26.30-Manufacture of ceramic tiles and flags" (14,433), "28.75-Manufacture of other fabricated metal products n.e.c." (11,552) and "28.51-Treatment and coating of metals" (8,192). In the Center (C) of Italy, the sectors in list A with the highest number of potentially exposed are "28.75-Manufacture of other fabricated metal products n.e.c." (6,233), "26.70-Cutting, shaping and finishing of stone" (4,905) and "26.21-Manufacture of ceramic household and ornamental articles" (4,009), while in the South and Islands (SI) area "28.75-Manufacture of other fabricated metal products n.e.c." (5,097), "26.70-Cutting, shaping and finishing of stone" (4,593) and "45.23-Construction of highways, roads, airfields and sport facilities" (3,458).

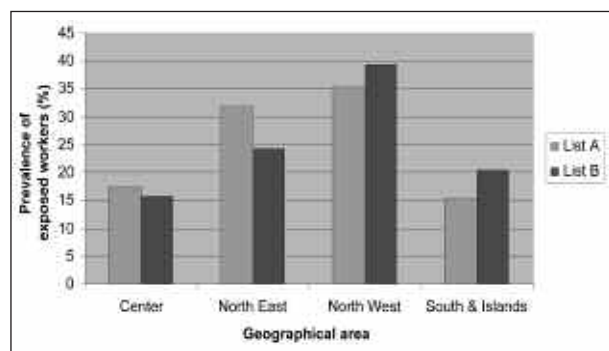
As regards list B, the activity sectors with a greater number of exposed workers are: "34.10-Manufacture of motor vehicles" (27,281 blue-collars) for

Table 1. Number of firms and workers (blue and white-collars) belonging to List A and B by economic activity (section and subsection)

Economic activity	List A			List B		
	Firms	Blue-collars	White-collars	Firms	Blue-collars	White-collars
C Mining and quarrying	1,806	8,217	3,708	-	-	-
DA Manufacture of food products, beverages and tobacco	-	-	-	2,663	26,350	10,196
DC Manufacture of leather and leather products	-	-	-	2,000	18,503	6,471
DD Manufacture of wood and wood products	-	-	-	11,016	29,266	22,617
DE Manufacture of pulp, paper and paper products; publishing and printing	-	-	-	8,253	42,566	28,472
DF Manufacture of coke, refined petroleum products and nuclear fuel	14	133	158	-	-	-
DG Manufacture of chemicals, chemical products and man-made fibres	1,126	12,325	7,854	79	962	3,035
DH Manufacture of rubber and plastic products	-	-	-	1,324	22,354	8,511
DI Manufacture of other non-metallic mineral products	8,412	59,583	27,990	2,550	22,988	9,371
DJ Manufacture of basic metals and fabricated metal products	15,102	90,538	43,858	-	-	-
DL Manufacture of electrical and optical equipment	78	737	310	-	-	-
DM Manufacture of transport equipment	1,443	12,308	5,801	2,410	125,064	37,038
E Electricity, gas and water supply	1,210	6,952	9,855	-	-	-
F Construction	4,041	19,672	13,392	4,061	12,312	7,109
G Wholesale and retail trade; repair of motor vehicles, motorcycles and personal and household goods	-	-	-	41,730	76,398	71,985
I Transport, storage and communication	-	-	-	2,790	45,758	13,394
O Other community, social and personal service activities	-	-	-	4,898	17,900	6,681
Total	33,232	210,465	112,926	83,774	440,421	224,880

the NW, “50.20-Maintenance and repair of motor vehicles” (17,062) for the NE and (13,959) C, and “60.21-Other scheduled passenger land transport” (16,251) for the SI.

Concerning regional distribution in “industry and services”, Lombardy is at first place with 24% of exposed workers (50,100 blue-collars), followed by

**Figure 1.** Prevalence of exposed workers (blue-collars) by Italian geographical area for List A and B

Emilia-Romagna (30,133) and Veneto (28,395) with about 14% in relation to list A. For list B, Piedmont is the first region with 21% of exposed workers (91,034 blue-collars), followed by Lombardy with 17% (75,517) and Veneto with 11% (48,236). The distribution of exposed workers, of Texp (exposed workers rate) and Tdth (lung cancer death rate) by Italian province is shown in Table 2 (for provinces with the highest Texp value, and where Tdth value is greater than the Italian mean value of 55.83).

The correlation between Texp and Tdth results statistically significant ($p < 0.0001$) considering either the exposed workers (blue-collar) belonging to list A plus list B (Pearson's correlation coefficient $r = 0.41$) or those belonging only to list A ($r = 0.44$). The regression analysis finds a positive relationship between Texp and Tdth with a β coefficient of 0.02 ($p < 0.0001$) and r -squared of 0.2 for list A (see figure 2), and $\beta = 0.01$ ($p < 0.0001$), r -squared = 0.17 for lists A and B together. Residual analysis shows that the provinces of Porde-

Table 2. Number of workers belonging to List A and B, Texp (exposed workers rate) and Tdth (lung cancer death rate) by Italian provinces

Province ^a	Texp	Blue-collars (A)	Blue-collars (B)	Tdth	Tdth rank
Modena	1,904	12,069	8,195	62.30	37
Massa-Carrara	1,420	2,807	1,091	80.95	7
Verbano-Cusio-Ossola	1,344	2,138	1,268	76.08	14
Reggio nell'Emilia	1,185	5,378	4,041	64.99	30
Viterbo	1,088	3,142	784	69.95	21
Brescia	1,038	11,506	13,763	56.10	52
Lucca	804	2,994	2,139	67.70	24
Verona	760	6,285	10,415	56.50	50
Belluno	719	1,507	1,669	77.79	12
Vercelli	650	1,149	1,001	78.04	10
Bergamo	639	6,221	10,109	58.68	46
Como	624	3,355	5,085	58.98	44
Ravenna	616	2,142	2,543	76.47	13
La Spezia	580	1,252	1,088	71.78	18
Treviso	571	4,540	5,660	57.21	49
Cuneo	570	3,169	8,255	58.60	47
Novara	558	1,914	2,945	67.05	27
Padova	556	4,727	7,272	60.83	39
Varese	532	4,322	6,006	58.46	48
Sondrio	526	931	1,852	61.07	38
Perugia	512	3,102	4,840	56.44	51
Florence	490	4,572	10,509	58.90	45
Cremona	489	1,644	2,922	60.43	40
Bologna	486	4,447	9,517	67.96	23
Pavia	482	2,380	2,681	81.42	6
Ancona	453	2,030	3,279	59.76	41
Asti	447	931	2,596	64.80	31
Alexandria	439	1,835	3,896	81.77	4
Gorizia	437	596	1,083	84.25	1
Pistoia	434	1,166	1,558	63.31	36
Rovigo	426	1,032	1,334	82.46	2
Forli-Cesena	423	1,518	3,343	64.71	32
Udine	419	2,175	4,932	63.60	35
Ferrara	408	1,406	2,863	79.00	8
Lodi	396	782	1,430	65.26	29
Milan	381	14,121	26,071	67.25	25
Mantova	374	1,414	3,658	59.29	43
Parma	352	1,383	6,998	75.83	15
Biella	351	657	1,260	77.97	11
Venice	344	2,788	8,205	73.86	16
Rimini	337	919	1,884	72.25	17
Piacenza	330	871	3,064	67.08	26
Turin	324	7,020	69,813	67.00	28
Pisa	308	1,184	7,221	63.97	33
Genoa	297	2,607	2,438	78.69	9
Livorno	294	961	2,204	68.31	22
Savona	275	749	2,043	81.83	3
Terni	253	557	926	59.58	42
Grosseto	229	484	1,053	71.53	19
Trieste	223	541	1,630	81.74	5
Imperia	155	318	558	70.16	20
Rome	87	3,224	13,257	63.91	34

^aThe provinces with the highest Texp value, where Tdth value is greater than the Italian mean value (55.83)

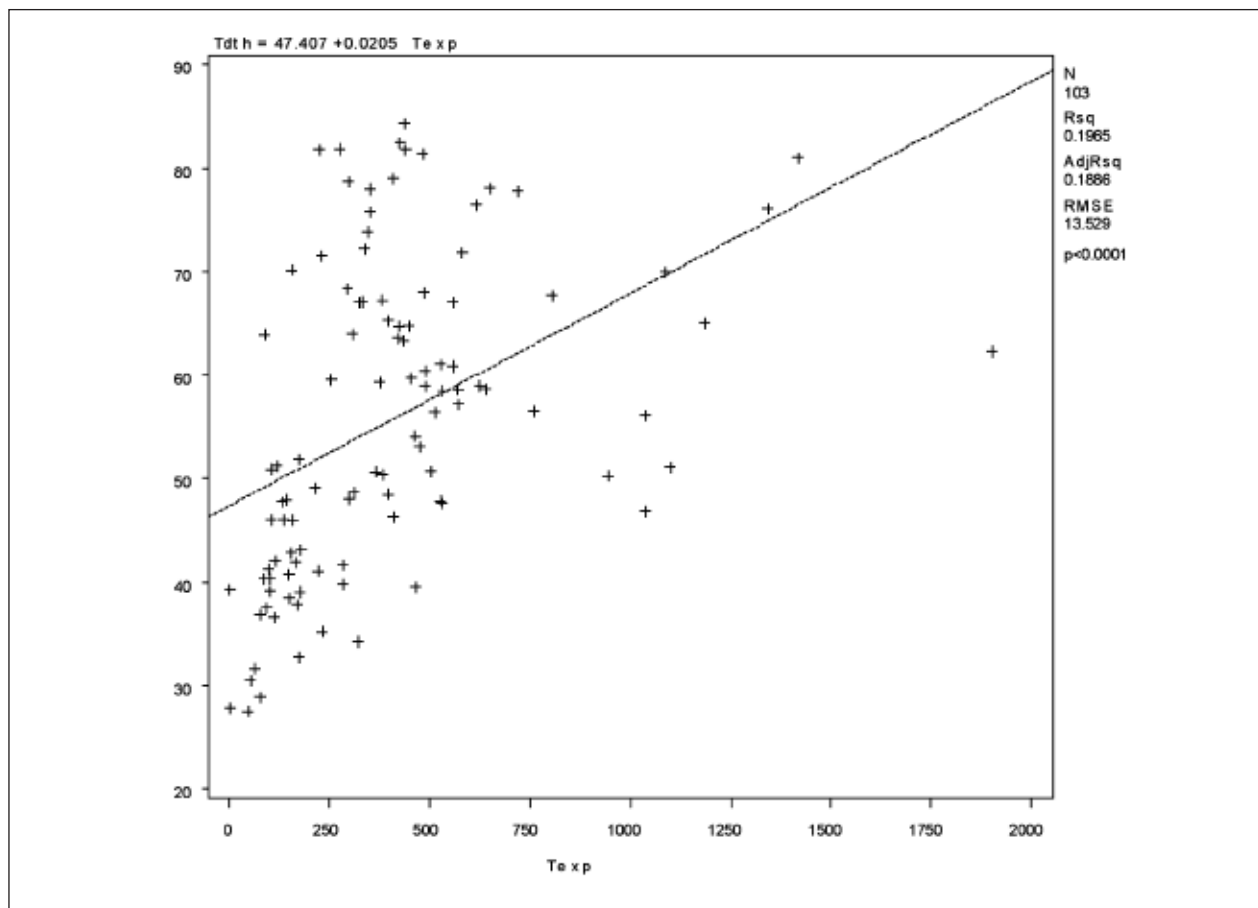


Figure 2. Regression analysis plot for List A. Tdth=lung cancer death rate; Texp= exposed workers rate

none, Lecco and Chieti (that have higher Texp values than the average) have Tdth values far less than expected by the regression model (more than the interquartile distance).

Discussion

The strengths and limitations of ISPESL database have been described elsewhere (15, 18). Briefly, it is necessary to remind the origin of the archives, which is represented by administrative-social security sources (20). The assessment of the number of companies and exposed workers is made through a procedure of “record-linkage”, instead of direct measurements of exposure levels. This kind of derivation im-

plies an inherent overestimation of the number of exposed workers. To avoid this problem, occupations made by blue-collar workers were considered separately from those made by white-collar workers. Indeed, white-collar workers include workers not directly exposed, like those employed in account and administration sections. The impossibility of being detailed in the industrial activity of enterprises, together with the possible wrong attribution of Ateco91 codes in the initial archives (INPS or UNIONCAMERE), represent a limitation of this study. Moreover, the poor specificity of some items within lists A and B (i.e. painters are not easy to be found in Ateco91 classification) could lead to an underestimation of exposed workers (13).

Some epidemiological studies make use of Job Exposure Matrices to estimate occupational exposure

risks (21, 22). In this study, the association between occupation and lung cancer risk (list A and B) is due to excesses documented in literature. An element in favour of the results validity is the restriction of research to those companies up to the third level of reliability, providing a further proof of certainty in relation to the number of employed workers.

The impossibility to know the occupation in detail, thus to consider as exposed workers all those qualified as blue-collars, including for example maintenance or supervision staff – generally exposed in a “different way” – is another limit of this study. An example is that not all the 19,433 workers of the economic sector “26.7-Cutting, shaping and finishing of stone” can be considered certainly exposed to carcinogenic agents. In any case, it is reasonable to suppose that this limitation does not influence the validity of results because this kind of specific jobs represent a small part of workers (23).

This study provides a contribution to the estimation of the oncogenic risk in working environments, considering the availability of complete administrative data for all companies recorded in the ISEPSL database. It is also necessary to take into account that a complete estimate of risks should integrate an assessment of ex-exposed workers.

In order to better understand the diffusion of lung cancer risk in Italy, it is necessary to have a look at the geographical distribution of exposed workers to lung cancer risk. The NW region has the highest percentage of blue and white-collars whose occupations entail or are likely to entail a risk of lung cancer, followed by the NE area. The C and SI have respectively the third place for list A and list B. This situation can be explained by the high percentage of mechanic industries and industries of manufacture of fabricated metal products, of non metalliferous minerals and construction of vehicles at risk of exposure especially in northern Italy.

Further studies, based on the lists, have been made for the north of Italy. A case control study has been conducted to assess the association between lung cancer risk, industries and occupations classified according to list A and B, in the north-eastern part of Italy. In particular, it has been analyzed the province of Trieste, where lung cancer mortality was higher than

in other Italian provinces (24, 25). The study has estimated that occupational lung cancer in the province population is 16% to 25% of the total lung cancer cases. The province presents many mechanic and metallurgical industries, as well as docks and shipyards, all occupational places which entail lung cancer risk for their workers. Specifically, a relevant lung cancer risk has been noted for shipyard and dock workers, carpenters and electricians, smelting/foundry workers, insulators and pipe coverers, due to the presence of asbestos in their workplace. Similarly, a higher lung cancer risk has been noted in iron, metal ware, gas and asphalt workers, in relation to their exposure to other carcinogens (mainly polycyclic aromatic hydrocarbons). Concerning list B, the occupations possibly entailing lung cancer risk are boilermakers, electricians, carpenters, plumbers, pipefitters, steamfitters, electrochemical workers, machinists and machine operators, mariners, mechanics, naval officers, railway and textile workers.

Interesting studies have been published on the Liguria region, in particular on the towns of Genoa and Savona (26-28), highlighting an excess of lung and respiratory tract cancers and diseases for shipyards and dockyards workers. Specifically, various working categories have resulted to be exposed to lung carcinogens. On the one hand, sectors like ship repair and refitting expose workers especially to asbestos, while shipbuilding to silica dust, naphtha, mineral oils, metal dusts, glass fibres and solvents. On the other hand, longshoremen are exposed to carbon oxide, PAHs and to hazardous substances contained in the cargo, such as carbon black or pesticides used to disinfect the ship. The Liguria region presents a high lung cancer risk also among refinery workers (29). In particular, maintenance and other blue-collar workers have been found to be highly exposed to hydrocarbons and asbestos, widely used as a thermal insulator for boilers and pipes.

Other studies (30, 31) have confirmed that in Piedmont the industrialized area of the city of Turin presents a high occupational lung cancer risk and an increased mortality rate for welders, metal workers, electricians and workers in electrical machine production, due to a high presence of foundries, mechanical and transport industries. Additionally, the province of

Alexandria is notorious for the asbestos cement plant of Casale Monferrato, which seems to account for the still existing high rate of lung cancer deaths (32).

Regression analysis indirectly validated our results, which suggest that the number of potentially exposed workers to lung cancer risk is associated with an increased prevalence of lung cancer deaths, this relationship being stronger for workers belonging only to list A (which represents the majority of economic activities related to occupational risk of lung cancer). Thus, working as blue-collar in an activity sector included in list A is a risk factor for lung cancer. The anomaly reported for some provinces (Pordenone, Lecco and Chieti), which have high values of Texp and low values of Tdth (far less than expected by the regression model), is due probably to commuting to work between neighbouring provinces.

The Italian situation of lung cancer exposed workers reflects the occupational condition of other industrialized countries. An interesting case-control study (33), based on lists A and B, has been made considering occupational exposure to lung cancer among non-smokers in seven European countries (France, Germany, Italy, Portugal, Spain, Sweden and UK). As a result, the research presents that the occupations belonging to list A with an excess risk of lung cancer for male workers are shipyard, dockyard, railroad manufacture working, painting and nonferrous metalliferous industry. Concerning list B, the most common occupations and industries suspected to entail lung cancer risk are carpentry, joinery, bus and truck driving, railroad working, vehicle manufacturing and repair. From the study, female workers result occupied especially in list B occupations and are possibly exposed to lung cancer when working in laundries or in rubber, ceramic, pottery and glass industries.

Data exhibited in this study indicate that more than 600.000 "industry and services" workers are occupationally exposed to lung carcinogenic agents, corresponding to 4% of Italian workers, in relation to last ISTAT census of "industry and services" (34). This estimate, described earlier (15), may be compared to the number of exposed workers to occupational carcinogenic agents derived by the European study CAREX, that has estimated 4 million workers to be potentially exposed in Italy (35, 36). To this

purpose, it has been used the review of publications made by Driscoll and colleagues for world mortality estimation of some professional cancers, such as lung cancer, on the basis of CAREX data and risk measures (37). The selected agents are: arsenic and compounds, asbestos, beryllium and compounds, cadmium and compounds, crystalline silica, diesel engine exhausts, hexavalent chromium and compounds, nickel compounds. Through these selecting criteria, it results from CAREX archive that 1.187.674 "industry and services" workers (excluding agriculture) were exposed in Italy to lung cancer risk during the period 2000-2003 (35). The distance between our estimation (650,886 exposed) and the one made by CAREX is mainly due to the selection criteria of worker categories considered as exposed. Indeed, our estimation is restricted to workers exposed to occupational cancer risk (blue-collars), whereas CAREX estimation could also include low-level exposures (38). Analyzing the whole occupational data from ISPESL archive, it results a total of 988,692 exposed workers (650,886 blue-collars and 337,806 white-collars). Thus, the difference between the estimates is considerably reduced.

Conclusions

The existence of a register of companies with activities linked to lung cancer risk, allows to plan territorial programs for prevention and surveillance related to industrial sectors mainly at risk, as well as explaining possible excesses in tumoral pathologies observed in the population. Furthermore, an archive which permits the identification and territorial localization of companies, through the Fiscal Code or Vat Number, could facilitate the activation of regional censuses with the aim of a real and detailed characterization of situations at high risk for the health of workers.

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