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# Residential proximity to industrial sites in the area of Taranto (Southern Italy). A case-control cancer incidence study

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**Summary.** The association between cancer incidence and the residence near polluting facilities in an industrial area nearby Taranto has been investigated. Age, sex and occupational exposure were controlled as confounding variables in a case-control study (658 cases, 2092 controls). High risks were evidenced close to the steel mill (OR: 3.54), coke plant (OR: 4.80), mineral deposit (OR: 3.33) and shipbuilding (OR: 4.29) for pleural neoplasm, and to the steel mill (OR: 1.65) and shipbuilding (OR: 1.79) for lung cancer. After adjustment for occupational exposure, increasing trends of risk were observed both for lung and bladder cancers. Cancer risks were evidenced near industrial sites and the introduction of "occupational exposure" as a confounder modified significantly the risks with respect to distance from the source of pollution, particularly for pleural, lung and bladder cancers.

*Key words:* air pollution, cancer, case-control study, Taranto, Italy.

**Riassunto** *(Residenza in prossimità di siti industriali nell'area di Taranto. Studio caso-controllo sull'incidenza dei tumori)*. È stata indagata l'associazione tra incidenza dei tumori e residenza in prossimità di siti inquinati tramite uno studio caso-controllo (658 casi, 2092 controlli) condotto nell'area industriale di Taranto. Le analisi sono state aggiustate per variabili confondenti (età, sesso ed esposizione occupazionale). Si è osservato un aumento del rischio per tumore della pleura in prossimità della cokeria (OR: 4,80), del deposito di minerali (OR: 3,33), dell'acciaieria (OR: 3,54) e dei cantieri navali (OR: 4,29), e in questi ultimi due siti anche per tumore del polmone (OR: 1,65 e 1,79). Aggiustando le stime per esposizione occupazionale si è osservato un aumento di rischio per i tumori del polmone e della vescica. L'introduzione dell'esposizione occupazionale come confondente ha modificato significativamente i rischi nelle distanze dalle sorgenti inquinanti, in particolare per i tumori della pleura, del polmone e della vescica.

*Parole chiave:* inquinamento atmosferico, tumore, studio caso-controllo, Taranto, Italia.

## INTRODUCTION

Taranto is one of the areas identified at high risk of environmental crisis in Italy because of a wide industrial area developed nearby the urban settlement, with a high population density [1]. The industrial zone is characterized by the presence of various types of plants, namely: one of the greatest steel mills in Europe, a major oil refinery, shipbuilding, a navy arsenal, a cement plant, two thermoelectric power plants and other plants for the manufacturing of rubber and plastic products, industrial chemicals, miscellaneous products of petroleum and coal, metal products, electric and electronic machinery and equipment. Such industrial activities are responsible for environmental contamination, mainly due to heavy metals, asbestos, polycyclic aromatic hydrocarbons (PAHs), organic solvents, polychlorinated biphenyls (PCBs) and dioxin. On this ground, Taranto has been included in the list of polluted sites of national interest in order to implement environmental remediation [2].

Specific studies of assessment of air emissions have been carried out in Taranto, in particular for suspended particulate matter in the neighborhood of steelworks, cement production and refinery plants, and for PAHs, benzo(a)pirene, heavy metals deriving from the steel foundry's coke-oven batteries and from

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the municipal solid waste incinerator [3-7]. Occupational exposure to PAHs and inorganic arsenic has been investigated through biological monitoring on a sample of workers [8, 9]. The first epidemiological study, on the basis of a ecological design, on the health status of population resident in Taranto was carried out by WHO in 1997 [10]. Other studies followed in 2002 and 2007 [11, 12]. All studies considered mortality data and results showed rates for all-causes and all-cancers higher than regional mortality rates. Significant excesses were observed for lung, pleura, bladder, liver and lymphohematopoietic system. No further studies, considering incidence cancer figures and occupational exposure as confounder in performing environmental risk estimates, have been published.

The aim of the study, designed as a case-control, is to investigate the association between the residence near selected polluting facilities in the municipality of Taranto – as proxy of environmental exposures – and the incidences of lung cancer, pleural neoplasm, lymphohematopoietic system malignancies and bladder cancer.

## SUBJECTS AND METHODS

The present survey was designed as a case-control study. Cases were selected from Hospital Discharge Records (HDRs) archives for the period 1998-2002. Incident cases were defined as those discharged during the period 2000-2002 and prevalent cases were excluded considering for each case those presenting the same disease in the previous 2 years. Incident cases, resident in the municipality of Taranto, in the period 2000-2002, were 743. According to the ICD-IX revision, cancer sites included in this study were: lung cancer (162.0-162.9), pleural neoplasm (163.0-163.9), lymphohematopoietic system malignancies (200.0-208.9) and bladder cancer (188.0-188.9). Metastases were controlled for lung and pleura considering the five codes reported in the HDR: if together with code 162 or 163 is reported another cancer site, the first is discarded as metastasis and considered as valid the new one.

Controls, in the number of 2229, resident in the same area at the end of 2002, were randomly sampled from Regional Health Service. The distribution of controls was stratified by sex and age (35-74, five years age classes) and matched by frequency with the corresponding distribution among cases, with a ratio of 1:3. Residential histories of all study subjects (2972) were collected through the Census Registry Office of Taranto and 222 subjects were excluded because without a detailed residential history (85 cases and 137 controls).

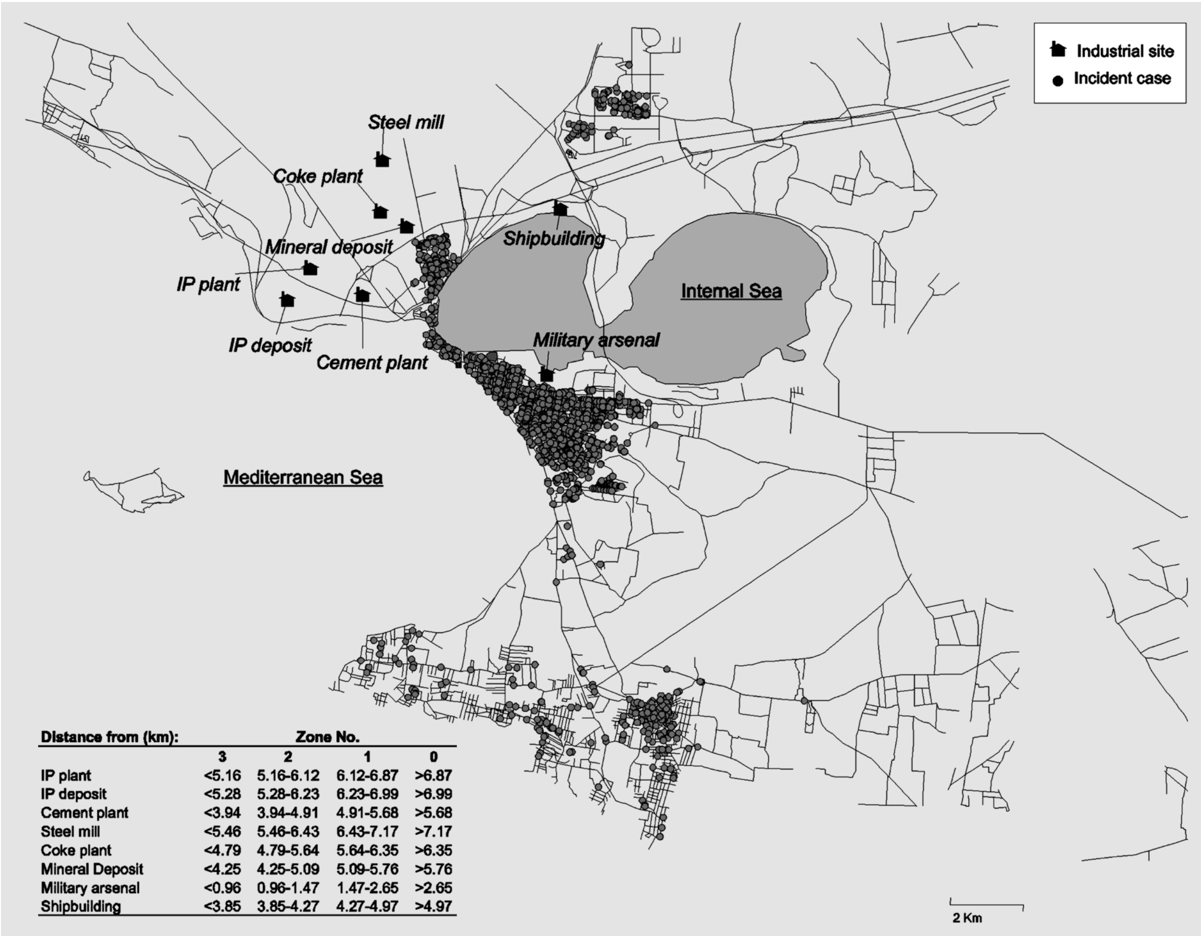
The majority of subjects were born and raised in Taranto province (77.2%), mostly in Taranto municipality (67.2%). The longest held residence, with the exclusion of the last ten years, was defined as the main residence of each subject and was reported on a digitalized map of the study area using MapInfo mapping software (www.mapinfo.com). A total of eight possible sources of industrial environmental pollutants in the Taranto municipality were considered: petroleum refinery plant, petroleum deposits, cement plant, mineral deposit, coke plant, steel mill, shipbuilding area, military arsenal. Controls without detailed information on residence have been excluded and HDRs have been controlled to exclude metastases and to reduce misclassification bias.

Distances between the main residence of each study subject and the central point of each source were computed and grouped into quartiles to define four zones, concentric with the central point of each source (from 0 zone, the furthest, to 3 zone, the closest) and equivalent in terms of the amount of resident population *(Figure 1)*. Industrial activity of cases and controls was retrieved from the Italian Social Security Institute (INPS) files for each study subject, throughout a record linkage with the personal identification number (CF), that in Italy means an individual code generated from the name, surname, sex, date and place of birth.

Employment histories for workers in private companies were identified in INPS files which collect the name of employing company and the industrial sector codes in which it operates and the period of employment. Each individual is considered as "exposed" to a given industrial sector if he/she worked for a company in that sector for at least a year and as "unexposed" if employed in banks, shops, hotels and restaurants, insurance, education and social services. If an individual is employed in different sectors for more than one year, the longest period of employment was considered.

More details about linkage procedure with INPS files, are described elsewhere [13].

Economic activities playing a "certain" or "suspected" etiological role were selected for each of the four cancer sites in the study, on the basis of strong evidences resulting from scientific literature (*e.g.* shipbuilding, chemical, steel, construction, metal mining and processing, glass and ceramic industries for lung cancer; building, shipyards, railway stock, metal, asbestos-cement and asbestos insulation industries for pleural neoplasm; rubber, cable and dyestuff manufacture, textile, leather, shoemaker, chemical, steel, pharmaceutical and print industries for bladder cancer; chemical industry, oil extraction and refinery, electricity production and transports for lymphohematopoietic system malignancies). Next, a matrix of association between each economic activity sector identified (coded according to the Italian ATECO81 classification, in-line with the European standard classification NACE70) and the four cancer sites was created, assigning three different levels of occupational exposure to carcinogens in the aforementioned economic sectors of activity: "no exposure", "possible exposure", "certain exposure" (*e.g.* in metal mining and processing industries: "certain exposure" for lung cancer, but "no exposure" for pleural neoplasm and "possible




| Distance from (km): | Zone No. | | | |
|---|---|---|---|---|
| | 3 | 2 | 1 | 0 |
| IP plant | <5.16 | 5.16-6.12 | 6.12-6.87 | >6.87 |
| IP deposit | <5.28 | 5.28-6.23 | 6.23-6.99 | >6.99 |
| Cement plant | <3.94 | 3.94-4.91 | 4.91-5.68 | >5.68 |
| Steel mill | <5.46 | 5.46-6.43 | 6.43-7.17 | >7.17 |
| Coke plant | <4.79 | 4.79-5.64 | 5.64-6.35 | >6.35 |
| Mineral Deposit | <4.25 | 4.25-5.09 | 5.09-5.76 | >5.76 |
| Military arsenal | <0.96 | 0.96-1.47 | 1.47-2.65 | >2.65 |
| Shipbuilding | <3.85 | 3.85-4.27 | 4.27-4.97 | >4.97 |

**Fig. 1** | *Spatial distribution and distance zones from industrial sites in Taranto area.*

exposure" for bladder and lymphohematopoietic system cancers). Therefore, a certain or possible or absent occupational exposure for each subject of the study has been defined. This matrix was revised from a panel of experts considering results of the OCCAM procedures and the suggestions of an "in-progress" matrix for occupational cancer recognition [14].

Odds ratios (ORs) for the selected cancer sites, associated with the four distances from each industrial site, were estimated by use of the STATA package (www.stata.com). Each subject of the study has been assigned to one of the four concentric zones and risk estimates have been calculated assuming the 0 zone as reference in all the associations. Risk estimates were adjusted for sex, age and occupational exposure (as defined above), in order to verify the possible confounding effect of workplace exposure on risk estimates for environmental exposure. Adjusted ORs and their 95% confidence intervals were estimated by the Mantel-Haenszel procedure. P-trend analyses were also computed to verify the trend of risk across the four zones for each association between industrial site and cancer risks.

## RESULTS

The study included 658 cases (509 males and 149 females) and 2092 controls (1608 males and 484 females). Economic activity sectors were identified in INPS files for 1104 subjects (40.1% of all study subjects) and 669 workers (24.3%) were definitely included, having at least 12 months of occupational history ascertained. The occupational sector assigned to each worker was the one with the longest duration (weeks). For both cases and controls the longest mean duration of exposure regards chemical (mean: 269.80; SD: ± 129.23), oil refinery (mean: 242.33; SD: ± 84.17) and steel (mean: 225.51; SD: ± 90.12) industries. By means of the linkage with INPS files, the economic activity sector was identified in 273 cases (41.5%) and 396 controls (18.9%).

The distribution of subjects by gender, age class and anatomical site is shown in *Table 1*. The association between occurrence of the selected tumours and the distances from the sources was evaluated for each industrial site. No statistically significant risk estimates were detected in associations with any distance from four of the investigated facilities: oil refinery, oil deposits, cement plant and navy arsenal. Consequently no table has been reported for these associations. At least one statistically significant association was found with each of the three major facilities of the metal industry site (steel mill, coke plant, mineral deposit) and with the shipbuilding industry. *Table 2* and *Table 3* show risk estimates for pleural neoplasm, lung cancer, lymphohematopoietic malignancies and bladder cancer by decreasing distances from the aforementioned industrial sites.

High risks for pleural neoplasm were observed in zones 2 and 3 from steel mill, coke plant, mineral deposit, and also in zone 1 from shipbuilding *(Table 2)*.

When adjusting ORs for occupational exposure, decreased values were observed in the three zones from each industrial site (except for zone 1 from shipbuilding), showing a strong confounding effect of occupational exposure on risk estimates, although statistical significance was never reached at 95% confidence level *(Table 2)*.

Positive associations were observed between lung cancer and distances from the selected industrial sites, with statistically significant ORs for steel mill (zones 2, 3) and shipbuilding (zone 2). The highest values were found in zones 2, supposing a greater risk at a medium distance from the source of pollution, rather than at the nearest or farthest. After adjusting for occupational exposure, increased values were found in most of the zones from the industrial sites, again with the highest in zones 2 where they reach also the statistically significance at 95% confidence level *(Table 2)*, implying a possible stronger contribution of environmental exposure in lung cancer risk. P-trend analyses confirmed at a statistically significant level the quadratic form (p = 0.045) of the trend in the zone 2 from shipbuilding.

No clear risk effect regarding lymphohematopoietic malignancies and bladder was found at any distance from the industrial sites *(Table 3)*.

## DISCUSSION

Before any consideration of the study findings, a preliminary discussion is due, regarding the quality of pathology data used. HDRs archives were used to identify incident cases and are diffuse in electronic format over almost the whole national territory in Italy, as well as mortality data (which are not adequate when considering malignancies with high survival). Classification and coding criteria are standardized, but data quality is lower when compared to population tumour registers which, on the other hand, cover only a minor part of the Italian population, HDRs are archived in Regional databases and are available with only a 6-months delay. Though a misclassification bias is possible for cancer sites with an high percentage of metastatic infiltration (pleura and lung), HDRs for lung, bladder and leukaemia have been recently demonstrated to be appropriate to detect incident cases [13].

The environmental exposure to emissions from the industrial sites considered in the study has been indirectly estimated by the distances from each site, and this could be a limitation for the study design. Information about residential histories of all study subjects was collected through the Census Registry Office of Taranto. We define the longest residence, with exclusion of the last ten years, as the "main residence". This exclusion sounds rather reasonable when considering neoplasms with significantly different latencies, ranging from 40 years for pleural cancers to 10-15 years for bladder and lymphohematopoietic neoplasms, but does not account for calendar years of residence, in which different patterns of exposure could have occurred. The unavailable distribution of residences according to age could have introduced some exposure misclassification, especially if the longest held was typically the childhood residence.

The analysis of confounding variables has been carried out in the absence of any information col-

**Table 1** | *Distribution of cases and controls by sex, age class and anatomical site (N, %)*

| Age class | Pleura | | | | Lympho-Hematopoietic | | | | Lung | | | | Bladder | | | | Controls | | | | Total | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | M | | F | | M | | F | | M | | F | | M | | F | | M | | F | | M | | F | |
| | N | % | N | % | N | % | N | % | N | % | N | % | N | % | N | % | N | % | N | % | N | % | N | % |
| 35-39 | - | | - | | 1 | 0.9 | 3 | 3.7 | 2 | 0.9 | 1 | 2.9 | 1 | 0.6 | - | | 15 | 0.9 | 11 | 2.3 | 19 | 0.9 | 15 | 2.4 |
| 40-44 | 1 | 6.7 | 1 | 12.5 | 4 | 3.6 | 4 | 4.9 | 2 | 0.9 | 2 | 5.9 | 3 | 1.9 | 1 | 4.0 | 31 | 1.9 | 25 | 5.2 | 41 | 1.9 | 33 | 5.2 |
| 45-49 | - | | 1 | 12.5 | 9 | 8.2 | 11 | 13.4 | 11 | 4.9 | 1 | 2.9 | 6 | 3.8 | 3 | 12.0 | 79 | 4.9 | 51 | 10.5 | 105 | 5.0 | 67 | 10.6 |
| 50-54 | 2 | 13.3 | 1 | 12.5 | 9 | 8.2 | 5 | 6.1 | 22 | 9.7 | 4 | 11.8 | 9 | 5.7 | 2 | 8.0 | 140 | 8.7 | 39 | 8.1 | 182 | 8.6 | 51 | 8.1 |
| 55-59 | - | | 1 | 12.5 | 13 | 11.8 | 12 | 14.6 | 23 | 10.2 | 3 | 8.8 | 28 | 17.7 | 1 | 4.0 | 205 | 12.7 | 57 | 11.8 | 269 | 12.7 | 74 | 11.7 |
| 60-64 | 2 | 13.3 | - | | 19 | 17.3 | 10 | 12.2 | 40 | 17.7 | 5 | 14.7 | 25 | 15.8 | 6 | 24.0 | 264 | 16.4 | 78 | 16.1 | 350 | 16.5 | 99 | 15.6 |
| 65-69 | 3 | 20.0 | 3 | 37.5 | 18 | 16.4 | 17 | 20.7 | 54 | 23.9 | 9 | 26.5 | 38 | 24.1 | 6 | 24.0 | 366 | 22.8 | 113 | 23.3 | 479 | 22.6 | 148 | 23.4 |
| 70-74 | 7 | 46.7 | 1 | 12.5 | 37 | 33.6 | 20 | 24.4 | 72 | 31.9 | 9 | 26.5 | 48 | 30.4 | 6 | 24.0 | 508 | 31.6 | 110 | 22.7 | 672 | 31.7 | 146 | 23.1 |
| Total | 15 | 100.0 | 8 | 100.0 | 110 | 100.0 | 82 | 100.0 | 226 | 100.0 | 34 | 100.0 | 158 | 100.0 | 25 | 100.0 | 1608 | 100.0 | 484 | 100.0 | 2117 | 100.0 | 633 | 100.0 |

**Table 2** | *Adjusted ORs for pleural neoplasm and lung cancer according to the distance from industrial sites*

| | Pleural neoplasm | | | | Lung cancer | | | |
|---|---|---|---|---|---|---|---|---|
| Industrial sites (zone) | Cases | Controls | Adjusted OR[a] (95% CI) | Adjusted OR[b] (95% CI) | Cases | Controls | Adjusted OR[a] (95% CI) | Adjusted OR[b] (95% CI) |
| **Steel Mill** | | | | | | | | |
| 0 | 3 | 529 | 1.00 | 1.00 | 47 | 529 | 1.00 | 1.00 |
| 1 | 0 | 511 | - | - | 69 | 511 | 1.48 (1.00-2.19) | 1.15 (0.56-2.38) |
| 2 | 9 | 529 | 2.81 (0.74-10.71) | 1.02 (0.16-6.42) | 75 | 529 | 1.65 (1.12-2.44) | 2.87 (1.43-5.79) |
| 3 | 11 | 523 | 3.54 (1.03-12.17) | 1.62 (0.37-7.10) | 69 | 523 | 1.49 (1.01-2.22) | 1.88 (0.92-3.87) |
| **Coke Plant** | | | | | | | | |
| 0 | 2 | 520 | 1.00 | 1.00 | 53 | 520 | 1.00 | 1.00 |
| 1 | 2 | 523 | 0.89 (0.13-6.13) | 0.30 (0.01-6.38) | 71 | 523 | 1.29 (0.88-1.88) | 0.90 (0.45-1.79) |
| 2 | 10 | 524 | 4.80 (1.07-21.62) | 2.89 (0.39-21.28) | 72 | 524 | 1.35 (0.93-1.98) | 2.05 (1.07-3.93) |
| 3 | 9 | 525 | 4.35 (0.95-19.99) | 2.18 (0.31-15.31) | 64 | 525 | 1.18 (0.80-1.75) | 1.45 (0.74-2.81) |
| **Mineral Deposit** | | | | | | | | |
| 0 | 3 | 527 | 1.00 | 1.00 | 53 | 527 | 1.00 | 1.00 |
| 1 | 1 | 519 | 0.31 (0.03-2.86) | - | 71 | 519 | 1.32 (0.90-1.93) | 0.91 (0.45-1.81) |
| 2 | 10 | 521 | 3.33 (0.92-12.12) | 1.56 (0.31-7.87) | 73 | 521 | 1.43 (0.96-2.09) | 2.06 (1.08-3.94) |
| 3 | 9 | 525 | 2.91 (0.80-10.65) | 1.17 (0.24-5.58) | 63 | 525 | 1.18 (0.80-1.75) | 1.38 (0.71-2.69) |
| **Shipbuilding** | | | | | | | | |
| 0 | 2 | 521 | 1.00 | 1.00 | 51 | 521 | 1.00 | 1.00 |
| 1 | 3 | 519 | 1.60 (0.27-9.44) | 2.83 (0.27-29.36) | 54 | 519 | 1.07 (0.71-1.61) | 1.15 (0.57-2.32) |
| 2 | 9 | 521 | 4.27 (0.89-20.58) | 1.26 (0.12-12.99) | 89 | 521 | 1.79 (1.23-2.59) | 2.25 (1.16-4.36) |
| 3 | 9 | 531 | 4.29 (0.94-19.53) | 2.82 (0.41-19.69) | 66 | 531 | 1.29 (0.87-1.90) | 1.57 (0.79-3.15) |

*a: OR adjusted for sex and age class.*
*b: OR adjusted for sex, age class and professional exposure.*

lected by interviews. Our information come from existing files, thus preventing recall bias. Age and gender were available by HDRs archives and checked by administrative files. No information about smoking habits or education level was available. In order to verify the occupations of cases and controls a linkage has been implemented with INPS archives supposing the same distribution of cases and controls in the non-matched subjects, that likely introduces a reasonable limit to the study design.

Nevertheless missing information on occupational histories may occur, due to a link failure or to unrecorded data. Indeed, INPS files record pension data only of employees of private firms, excluding self-employees. Moreover, INPS archives do not include the agriculture sector, the public administration and the Department of Defence. Data are available electronically only since 1974. On the other hand, the INPS files allow to reconstruct the whole work history of each subject and not only the last one. Contribution periods have been retrieved for the 24.3% of the subjects (cases or controls) included in the study. This percentage is to be intended as relevant if we consider that – for the first time in Italy – such archives have been used to find back employment histories in an environmental case-control study, thus substituting individual information collected by interviewers. In planning future research at national level this opportunity (cheaper and less time-consuming with respect to personal interviews) should be considered. However, additional registration, allowing the reconstruction of personal work histories should be integrated in order to enlarge the amount of subjects to be included, the statistical power of risk estimate analyses. The absence of information about working periods in the Department of Defence could introduce some bias given that Taranto area presents a large amount of navy workforce (2000-2500 employed, whereof around 600 permanently), possibly having an impact on risk estimates for specific cancer sites (lung, pleural mesothelioma, lymphohematopoietic system).

Furthermore, considering only the longest held job may introduce a residual confounding of results and it is not easy to identify the specific source of contamination considering the large overlapping among the distance zones of industrial sites.

Many authors studied the association between air pollution and lung cancer: case-control studies and geographic analyses have been performed, providing useful elements to evaluate the etiologic role of air pollution. A significant association between lung cancer, residence near industrial sites (smelters, complex industrial areas, steel and chemical industries), and air pollution were described [15-19]. Other studies showed an increased risk of mesothelioma in relation to residential proximity to industrial sources of asbestos, namely: asbestos cement plants, asbestos mines, shipyards, or other factories [20-22].

Recently a large mortality analysis was conducted in the Taranto area, evidencing a significant excess of mortality for lung, pleura and bladder cancer and cirrhosis in the period 1970-2004 [23]. Our study, confirming these findings, provides more detailed discussion points. We find a significant pleural cancer incidence risk for subjects who lived near the steel mill and coke plant. The proximity to mineral deposit and shipbuilding is predictive of a major risk but, as a consequence of the small sample size, statistical significance is not reached. For all sites, an evident "bounce effect" is remarked: the relative risk is, almost ever, higher for the zone 2 than for the zone 3 (that is the nearest to the industrial sites). The occupational etiology of a large part of pleural cancer cases is showed indirectly by the decrease of relative risks after adjusting risk estimates for occupational exposure (as described in the methods). The Taranto area has been one of the most relevant sites using asbestos in Italy (until the total ban in 1992) in the shipbuilding and repair and in the steel mill plant (two industrial sectors that have strongly oriented the economy and the labour force scenario in the area) and the excesses for pleural cancer detected seem to be partly explained by an occupational origin [24].

As far as lung cancer is considered, we find a significant risk excess referable to the residence near the steel mill and shipbuilding. There is a clear shaped trend of the estimated risk with a peak for zone 2 with respect to all industrial sites. The pattern of risk estimates seems to follow a specific trend, where living at medium distance from the source of pollution appears of more risk than near-source. The interpretation of such results should be devolved to complex atmospheric dispersion models that should support the arrangement of next environmental studies in the area [25]. When controlling occupational exposure as confounder in risk analyses, results showed increased values (most evident in the zones 2), suggesting a remarkable "pure" residence effect where the environmental contribution to lung cancer risk appears stronger (in contrast with pleural cancer risks).

No clusters of lymphohematopoietic malignancies

**Table 3** | *Adjusted ORs for lymphohematopoietic malignancies and bladder cancer according to the distance from industrial sites*

| | Lymphohematopoietic malignancies | | | | Bladder cancer | | | |
|---|---|---|---|---|---|---|---|---|
| **Industrial sites (zone)** | **Cases** | **Controls** | **Adjusted OR[a] (95% CI)** | **Adjusted OR[b] (95% CI)** | **Cases** | **Controls** | **Adjusted OR[a] (95% CI)** | **Adjusted OR[b] (95% CI)** |
| **Steel mill** | | | | | | | | |
| 0 | 49 | 529 | 1.00 | 1.00 | 47 | 529 | 1.00 | 1.00 |
| 1 | 52 | 511 | 1.12 (0.74-1.69) | 0.72 (0.33-1.57) | 40 | 511 | 0.87 (0.56-1.35) | 1.11 (0.52-2.35) |
| 2 | 40 | 529 | 0.80 (0.51-1.24) | 0.48 (0.21-1.13) | 53 | 529 | 1.11 (0.73-1.67) | 1.28 (0.60-2.72) |
| 3 | 51 | 523 | 1.08 (0.71-1.64) | 0.66 (0.32-1.40) | 43 | 523 | 0.95 (0.61-1.46) | 1.46 (0.68-3.12) |
| **Coke plant** | | | | | | | | |
| 0 | 49 | 520 | 1.00 | 1.00 | 48 | 520 | 1.00 | 1.00 |
| 1 | 49 | 523 | 1.03 (0.68-1.57) | 0.71 (0.33-1.51) | 42 | 523 | 0.86 (0.56-1.33) | 1.14 (0.54-2.42) |
| 2 | 44 | 524 | 0.88 (0.57-1.35) | 0.64 (0.28-1.48) | 52 | 524 | 1.03 (0.68-1.56) | 1.36 (0.63-2.93) |
| 3 | 50 | 525 | 1.04 (0.68-1.57) | 0.51 (0.24-1.11) | 41 | 525 | 0.86 (0.56-1.34) | 1.18 (0.56-2.49) |
| **Mineral deposit** | | | | | | | | |
| 0 | 51 | 527 | 1.00 | 1.00 | 47 | 527 | 1.00 | 1.00 |
| 1 | 49 | 519 | 1.02 (0.67-1.54) | 0.82 (0.39-1.71) | 47 | 519 | 1.00 (0.66-1.54) | 1.19 (0.56-2.52) |
| 2 | 42 | 521 | 0.81 (0.52-1.24) | 0.48 (0.20-1.18) | 48 | 521 | 1.00 (0.65-1.52) | 1.26 (0.58-2.74) |
| 3 | 50 | 525 | 0.99 (0.66-1.50) | 0.52 (0.24-1.12) | 41 | 525 | 0.90 (0.58-1.39) | 1.17 (0.56-2.47) |
| **Shipbuilding** | | | | | | | | |
| 0 | 49 | 521 | 1.00 | 1.00 | 51 | 521 | 1.00 | 1.00 |
| 1 | 54 | 519 | 1.10 (0.72-1.66) | 0.87 (0.37-2.09) | 41 | 519 | 0.79 (0.51-1.22) | 0.72 (0.32-1.63) |
| 2 | 43 | 521 | 0.89 (0.58-1.37) | 0.62 (0.27-1.40) | 45 | 521 | 0.88 (0.58-1.34) | 0.93 (0.45-1.91) |
| 3 | 46 | 531 | 0.94 (0.61-1.44) | 0.69 (0.33-1.43) | 46 | 531 | 0.91 (0.60-1.39) | 1.54 (0.75-3.14) |

*a: OR adjusted for sex and age class.*
*b: OR adjusted for sex. age class and professional exposure.*

related to the main residence have been found (as well as for bladder cancer) and these findings seem to be consistent considering the relevant sample size. The characteristic shape with a peak of risk for zone 2 is present also for bladder but not for lymphohematopoietic cancer.

## CONCLUSION

Due to the lack of emission data for the study period, we have considered the residence of case and controls as a proxy index of environmental exposure including the economic sector of activity as a "occupational" confounder in the analyses of environmental risk estimate. Any reduction of the risk estimates following the introduction of the occupational exposure in the model suggests a role of the occupational component in the associations considered (*e.g.* pleural neoplasm risk and residence close to the steel mill and coke plant). On the other hand, any reduction of the risk estimates following the adjustment for the occupational variable could suggest a more important role of environmental exposures in determining specific associations (*e.g.* lung cancer risk and residence near the steel mill, the mineral deposit and the shipbuilding, confirmed particularly in zone 2).

The p-trend analysis evidenced an increasing trend of cancer risk in zone 2, decreasing in zone 3, for lung cancer and the distance from the shipbuilding area. The employment of occupational information retrieved from INPS archives, seems reliable to track individual industrial activities, as well as the matrix of exposures by the panel of experts to define the different levels of occupational exposure. These issues provide useful additional tools in the design of further analytical epidemiological and environmental studies, using exposure quantitative measures.

### *Conflict of interest statement*

There are no potential conflicts of interest or any financial or personal relationships with other people or organizations that could inappropriately bias conduct and findings of this study.

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