Lung Cancer Mortality in a Cohort of Workers in a Petrochemical Plant: Occupational or Residential Risk?

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The purpose of the present study is to examine the role of environmental (non occupational) exposures in lung cancer risk among petrochemical workers at a large petrochemical plant built on the Sicilian coast in the immediate vicinity of the town of Gela, Italy in 1960. The cohort included workers employed in the Gela petrochemical plant in 1960–1993. We looked at mortality rates for the period 1960–2002. An internal comparison was performed between two categories of workers with different likelihood of residence in Gela during the period of employment. The rate ratio of mortality from lung cancer comparing "probable residents" with "possible non residents," adjusted for age, calendar period, and job classification (only blue collar, only white collar and both), was 1.66 (90% Confidence Interval 1.07–2.58). Although the information collected is quite sparse and no inferences can be made about risk sources, the results show a possible excess of residential/environmental risk from lung cancer mortality for those workers more likely to have been residents in Gela. *Key words*: cohort study; mortality; lung cancer; petrochemical industry; environment

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Several ecological studies conducted in the past 20 years showed an excess mortality from lung cancer among male residents in the municipality of Gela.[1-3] Gela is located on the seaside in the south west coast of Italy's Sicily Region, and is 20 or more kilometers distant from other municipalities.

The town of Gela underwent great changes in just a few years after 1956, when oil fields were discovered in its vicinity both onshore and offshore. Before that date, the town had approximately 40,000 inhabitants and its economy was mainly agricultural. In 1960, Gela was home to the largest petrochemical plant in Europe (as told by Enrico Mattei, the president of ENI, the National Board for Hydrocarbons). After a few years, the town and its surrounding territory had been completely transformed[4] and the population had grown by more than 50%. Nowadays, Gela is one of the largest Sicilian cities, with approximately 80,000 residents in 2001.

An extended area around Gela was declared "area at high risk of environmental crisis" in 1990.[5] In 1998 the area was deemed a "site of national concern for soil remediation" because of heavy chemical soil pollution from the large petrochemical plant.[6]

Today the industrial zone comprises a refinery capable of treating 5×10^6 tons of oil per year; a power plant; and a number of chemical plants that produce a variety of chemicals, polymers, and agricultural products, as well as phosphoric and sulphuric acids. The power plant is fuelled by "pet-coke," a residual by-product of the oil-refining process. It is a fossil fuel that contains varying amounts of chemical agents such as sulphur, mercury, nitrogen oxides, and vanadium.

Two recent studies on particulate matter (pine needles and road dust samples) showed that the entire area of Gela is heavily affected by industrial and urban emissions of metals and metalloids.[7,8]

Some researchers[2] have suggested occupational exposures as a possible cause of increased mortality from lung cancer among males residents in Gela.[1–3] Here we examine the role of environmental (non-occupational) risk factors for lung cancer in Gela.

BACKGROUND

Lung Cancer Risk Among Petrochemical Workers

The plausibility of lung cancer risk among workers in petrochemical plants, and in chemical industry as a whole, is supported by some observations in occupational cohort studies. In studies from various countries, an increased lung cancer risk has been observed among petrochemical workers with prolonged duration in specific work categories, and/or with high exposure to specific chemicals.[9–12] Observed lung cancer risk is less than expected when petrochemical workers are studied without looking at specific work categories,[11] the Healthy Worker Effect may predominate and obscure the possible risk of specific subcohorts.[14] This is the general case for historical mortality cohort studies in which there is no categorization of workers

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by specific exposures. Furthermore, in petrochemical settings, problems with exposure assessment due to the presence of chemical mixtures and variability of exposure in intensity and duration, may hamper the possibility of identifying risk increases.[15] In 2001, a meta-analysis of mortality and cancer experience of employees of the chemical industry in the United States and Western Europe, financed by the American Chemistry Council, revealed weak to moderate excesses of lung cancer that the authors attributed, at least in part, to previously reported associations to known human lung carcinogens (*e.g.* chromates).[16]

A previous analysis on Gela petrochemical cohort described mortality in terms of SMR (Standardized Mortality Ratio).[17] The SMR for lung cancer was 0.68 (N=66, 90% Confidence Interval, [CI]) 0.56–0.83). Duration of employment was not available from employment rosters. Most of the employees worked at various companies operating in the petrochemical plant in the study period. The job classification (only blue collar, only white collar, or both) was the only information available for internal cohort analysis. The rate ratio of mortality from lung cancer comparing only blue collar workers with only white collar workers, adjusted for age and calendar period, was 1.42 (90% CI 0.83–2.44). In comparing blue collar workers with white collar workers, an excess risk was observed for almost all causes of death. This finding was not easily interpretable and could be associated with differences in socioeconomic status (SES). The interpretation of findings on mortality in general and from lung cancer in particular, appears to be complex in epidemiological terms and is further complicated by observations of a sociological study, according to which in the years subsequent to the beginning of petrochemical activities, a great number of workers came from locations other than Gela (various provinces within Sicily as well as other Italian regions).[4]

Lung Cancer Risk in the Neighborhood of Petrochemical Plants

Evidence on lung cancer risk associated with residence in the neighbourhood of petrochemical plants is suggested by some studies. A higher risk of lung cancer was observed in residents of the most polluted areas in the region of Teeside, U.K., where petrochemical, steel and other industries are located.[18] A case control study among women carried out in the same region produced analogous results.[19] An association between risk of lung cancer and residence near petrochemical plants was also observed in case-control studies performed in Louisiana, U.S.; in Taiwan; and in the town of Brindisi, Italy.[20–22] In these studies, the exposures from petrochemical industries were indirectly evaluated using as *proxy* distances of residences from the plants and duration of residence.

METHODS

The present study attempts to disentangle the effects of occupational and residential exposures by evaluating the possible contribution of residence in Gela to the risk of lung cancer among petrochemical plant workers.

Study Population

The initial study population was the same of the previous study of the Gela petrochemical cohort.[17] Twenty employment rosters from 8 companies were used to collect information on worker's personal and employment data. The cohort was composed of 6458 men, employed from 1960 (the year in which the plant operations started) to 1993, inclusive. Ascertainment of vital status was completed through a search at the individuals' municipality of residence and/or death for the years 1960–2002. The main source of data on death was the death certificate. Causes of death were coded by an expert nosologist according to ICD (International Classification of Diseases) rules in the year of death. No records were found for 4.1% of the total cohort and the cause of death could not be retrieved for 8% of deaths. The cohort analyzed in the present study was restricted to workers with no missing data on place of birth.

Residential History

Direct information on residential history of workers was not available . Data on residence at time of employment could be collected from company rosters but reconstruction of residential history was not possible, as rosters provided that information only for a specific point in time. Residence at hire was available for about 90% of the workers. However, this information was not considered reliable for workers who move to Sicily to work in the plant because there was no obligation to update resident status. Workers' place of birth was also available from employment rosters. This data can be considered valid because it was abstracted from identity documents (ID or driving licence); place of birth was obtained for almost all workers (98.5%).

We classified workers as "probable residents" and "possible non residents" on the basis of place of birth (Gela municipality, Sicilian municipalities other than Gela, municipalities outside Sicily) and on the assumptions that:

a) subjects who were born in Gela and had worked in the petrochemical plant were likely to have been residents in Gela at least during the employment period;
b) subjects who were born in Sicilian municipalities other than Gela may or may not have been residents in Gela during the employment period;

TABLE 1 Number and Proportion of Men Hired in the Period 1960–1993 by Place of Birth

	N° (%) by Period of Hire			
Place of Birth	**1960–1961**	**1962–1970**	**1970–1993**	**Total**
Gela	59 (21)	627 (18)	1,000 (37)	1,686 (26)
Other towns in Sicily	151 (56)	2,267 (66)	1,527 (56)	3,945 (61)
Outside Sicily	51 (19)	497 (14)	184 (7)	732 (11.5)
Missing	11 (4)	58 (2)	26 (1)	95 (1.5)
Total (%)	272 (4)	3,449 (53.5)	2,737 (42.5)	6,458

c) subjects who were born in municipalities outside Sicily were likely to have been residents in Gela at least in the period of employment in the petrochemical plant.

On the basis of the aforementioned assumptions, the workers were classified as "probable residents" if they were born in Gela or outside Sicily and "possible non residents" if they were born in a Sicilian municipality *other than* Gela. The plausibility of this categorization was supported by employment roster data on residence at hire of workers born in Sicily. The information on workers with data both on place of birth and residence at the time of employment, showed that 80% of workers born in Sicilian municipalities other than Gela were registered as resident in Sicilian municipalities other than Gela, while 98% of the workers born in Gela were registered as resident in Gela.

Statistical Methods

Mortality Rate Ratio (RR) for lung cancer, all neoplasms and all causes were estimated comparing workers by residence category and place of birth. A Poisson regression model, controlling RR for age, calendar period and job (categorized as blue collar, white collar, both blue and white collar), was applied using STATA 9.0 software. Confidence Intervals (CI) at 90% level were estimated by maximum likelihood method. For CI, 90% level was chosen to both focus on magnitude and precision of RR estimates and to limit the interpretation of CI as a significance test.[23]

RESULTS

Workers' provenance by period of employment in the entire cohort is described in Table 1. Most of the workers employed in the period 1960-1993 were hired in the first few years after 1960, 58% in the first 10 years. The proportion of workers born in municipalities outside Sicily in the first two years after plant opening was 19%. In the total cohort 26% of workers were born in Gela, 11.5% in municipalities outside Sicily and 61% in Sicilian municipalities other than Gela. We lacked information on place of birth for 1.5%. We obtained information on place of birth and job category for 5,911 workers. Of these, 2253 belonged to the "probable resident" category and 3,658 to the "possible non resident" category (Table 2).

Results of RR analysis are shown in Table 3. Comparing "probable residents" vs. "possible non residents," RR for all neoplasm is 1.13 (90% CI 0.88–1.46), for all causes 0.89 (90% CI 0.77–1.04), for lung cancer 1.66 (90% CI 1.07–2.58). Comparing lung cancer mor-

TABLE 2 Descriptive Data on Workers by Residence Category, "Probable Residents" and "Possible Nonresidents." Workers with Information on Place of Birth and Job (Blue Collar, White Collar or Both)

	Probable Residents		Possible Nonresidents
Place of Birth	**Gela**	**Outside Sicily**	**Other Towns in Sicily**
N	1,577	676	3,658
All deaths	105	86	346
Neoplasms	45	30	111
Lung cancer	17	12	29
Age at employment [a]	26 (14–55)	28 (19–55)	26 (17–57)
Age at the end of follow-up [a, b]	56 (23–91)	63 (24–86)	59 (22–91)
Latency [a, c]	30 (<1-43)	35 (<1–-43)	33 (<1–42)
Job (%)[d]			
Blue collar	1,067 (68)	150 (22)	1,917 (52)
White collar	188 (12)	473 (70)	990 (27)
Both	322 (20)	53 (8)	751 (21)

[a]Average (range)
[b]For dead workers age at death and excluding people lost to follow up (4%)
[c]Period from employment to the end of follow-up (duration of follow-up), excluding people lost to follow-up
[d]Column %

TABLE 3 Rate Ratio (RR) of Mortality from Lung Cancer, All Neoplasms, and All Causes, Comparing Workers by Category of Residence and Place of Birth. Workers with Information on Place of Birth and Job (Blue Collar, White Collar, or Both)

Cause of Death (IX ICD[c])	Category of Residence/ Place of Birth	RR[a]	90% CI
Lung cancer (162)	Possible non residents (ref)[b]	1.0	—
	Probable residents (a. & b.)	1.66	1.07–2.58
	a. Gela	1.51	0.9–2.51
	b. Outside Sicily	2.0	1.06–3.77
All neoplasms (140-208)	Possible non residents (ref) [b]	1.0	—
	Probable residents (a. & b.)	1.13	0.88–1.46
	a. Gela	1.04	0.78–1.4
	b. Outside Sicily	1.32	0.91–1.93
All causes (001-999)	Possible non residents (ref) [b]	1.0	—
	Probable residents (a. & b.)	0.89	0.77–1.04
	a. Gela	0.79	0.65–0.95
	b. Outside Sicily	1.08	0.87–1.35

[a]RR adjusted for age, calendar period and job (blue collar, white collar or both)
[b]Sicilian municipalities other than Gela
[c] International Classification of Disease IX revision codes

tality by place of birth using people born in Sicilian municipalities other than Gela as reference, RR is 1.51 (90% CI 0.9–2.51) for workers born in Gela and 2.0 (90% CI 1.06–3.77) for workers born in municipalities outside Sicily.

DISCUSSION

In the case of Gela, where a large petrochemical plant is the main source of environmental pollution, the mortality and/or morbidity analysis of workers can help elucidate environmental and residential risks, thus contributing to a greater understanding of the local epidemiological context. Results from our previous analysis of the petrochemical cohort showed a decreased mortality for all causes and also for lung cancer using Sicilian mortality as the reference.[17] For the Gela cohort, the defect in lung cancer risk could possibly be explained by the fact that smoking was strictly regulated since 1963 as shown by internal company documents.

Our current RR analysis comparing workers by category of residence could be affected by some bias. First of all, the categorization of residence is "intrinsically" affected by differential misclassification, because the likelihood that workers assigned to the category "possible non residents" were in fact residents of Gela is assumed to be greater than the likelihood that workers assigned to the category "probable residents" did not live in Gela. If differences in risk between groups are really due to differences in residence, the direction of misclassification would lead to a probable underestimation of RR comparing "probable residents" with "possible non residents." The analysis for lung cancer is not controlled for smoking because of lack of individual information on tobacco consumption. However, controlling for job could indirectly control for tobacco use and other dimensions of SES. Because usually blue collar work and, generally, lower SES status are associated with higher smoking prevalence,[24,25] controlling for blue collar versus white collar may partially control for smoking as a confounder.

One can argue that differences between the categories of residence defined according to our assumptions, could be due to different baseline risk of lung cancer by place of origin, due to varying environmental risk as well as lifestyle risks associated with different cultural habits. The SMR for lung cancer in the years 1999–2001 (with the whole of Italy as reference) is 1.11 in north western regions of Italy, 1.06 in the northern regions of Italy, and 0.84 in the island regions, one of which is Sicily.[26] Nevertheless, this fact could explain only a part of the observed excess in workers born outside Sicily (part of the "probable residents" category). The increased lung cancer risk among people born outside Sicily could partly be the result of exposures to occupational carcinogens in other plants or job outside Gela.

Lack of data on employment duration is another limitation in interpretation of the increased risk, because the excess risk in workers born in Gela could simply be due to longer employment in the industry and/or in specific job titles entailing a risk for lung cancer.

In spite of the limits and possible biases of this internal cohort analysis by place of birth, our results suggest a possible residential/environmental risk for lung cancer in workers of the petrochemical plant. Furthermore, this result is consistent with the epidemiological observation of the ecological analysis of mortality in Gela residents in the period 1995–2000, in which an excess of lung cancer was observed, not only in men (N=147, SMR 1.31, 95% CI 1.11–1.55) but also in women (N=23, SMR 1.43, 95% CI 0.91–2.14).[3]

CONCLUSIONS

The present results suggest a possible excess of residential/environmental risk of mortality from lung cancer for those petrochemical plant workers likely to have been residents in Gela. The information collected is quite sparse and no inferences could be made about risk sources. The Gela site remains classified as an areas with serious soil pollution, and remediation activities are ongoing, while so far no information on air pollution has been collected for the purpose of studying health effects.

The results of the present study are weak, but at the moment they are based on the best available and retrievable data on petrochemical workers. The present findings can thus be referred to in the frame of the "precautionary research,"[27] a notion that implies addressing issues of possible public health relevance even if the context might not be suitable for optimal study design. Implementing studies in areas where previous data were scanty may turn out to be useful for priority setting, both for environmental remediation, and for *ad hoc* epidemiological studies.

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