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Mortality study of cancer risk among oil refinery workers

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Summary. The mortality experience of 1595 male workers employed in one of the largest Italian refineries in the period from 1949–1982 was examined. From the comparison with national and local death rates, increases in mortality owing to lung and kidney cancers, brain tumors, and leukemias emerged. No definite trends according to duration of exposure and years since first exposure were apparent. The increases regarding cancer of the lung, kidney and brain appeared to be associated with the early period of operations. Analysis by exposure category suggested an association of the increased mortality from leukemias with working in production (observed = 2; expected = 0.61). Kidney cancer mortality was elevated among maintenance workers (obs. = 2; exp. = 0.18). Small numbers prevented firmer conclusions. Workers in the moving department had a significantly increased mortality from all cancers (obs. = 22; exp. = 11.7), and lung cancer (obs. = 11; exp. = 3.6). Confounding by smoking could be excluded as sufficient explanation of the three-fold increase in lung cancer deaths. It was in moving that highest airborne levels of polynuclear aromatic hydrocarbons had been discovered in an independent environmental investigation.

Key words: Polynuclear aromatic hydrocarbons (PAHs) – Epidemiology – Mortality – Occupational cancer – Oil refinery

Introduction

Petroleum and petroleum products have a complex composition. The principal constituents are hydrocarbons, some of which have been implicated by experimental, as well as epidemiological studies in the process of human carcinogenesis [19–22, 30]. Over the last decade, particular attention has been devoted to the possible cancer risk carried by exposures pertaining to working in petroleum refineries. Studies have been conducted in various settings and countries, and different approaches have been implemented: ecological investigations [6, 7, 13, 28], mortality [1, 9, 10, 14–17, 23, 29, 33, 35, 38–41, 43–47] and incidence [37] studies, and case-control studies [3, 4, 8, 25, 26, 34]. Despite certain limitations, mainly related to non availability of exposure data, and failure to control for confounding, these investigations have suggested possible cancer risks associated with working in oil refineries [36]. The findings, however, were not fully consistent, and further research was deemed necessary [18].

We thought it useful, therefore, to study the cancer mortality experience of the employees at a refinery plant located in the vicinity of Milan (Italy), one of the largest and earliest in the country, after verifying the availability of a good data source since the late 1940s. The aim of the study was twofold: to ascertain whether a cancer risk existed in that particular working population, and to investigate whether the risk, if any, was associated with specific jobs or plant processes and, hence, exposures.

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Subjects and methods

Study population. All male workers ever employed at the plant in any department between January 1, 1949 and December 31, 1982 were considered eligible. The examination of personnel files led to the identification of 1595 subjects meeting the admission criteria. Despite changes in the ownership of the plant, confidence could be placed on the complete enumeration of the cohort, since regulations in Italy require that a complete list of employees be kept for both administrative and compensation purposes. A double check with the individual records independently registered and stored at the plant health service strengthened this confidence. For each worker the following information was extracted: name, sex, place and date of birth, residence, date of entering and date of leaving the plant, and detailed work history inside the plant, viz. department(s), job(s), date in and out for each position held.

Exposure classification. The basic process at the refinery plant consisted of converting crude oil into a variety of hydrocarbon streams suitable for use as products directly or as blend components (solvents, fuels, lubricants).

Environmental data were collected in an independent survey, carried out between 1982 and 1985. Airborne contaminants were measured in typical positions, with the use of both personal and area samplers. Historical information on changes of production processes and their location within the plant was available since 1962. For the purposes of this study, 29 occupation units were identified on the basis of type of process, location inside the plant, characteristics of the job, and type of airborne contaminants. In order to achieve a meaningful size in each unit, a further grouping had to be made, and we ended up with the following categorization:

Production: this might indeed appear as a broad category. However, the majority of the relevant processes were controlled from a distance by a limited number of operators. Measurements of a number of chemicals had been performed (total hydrocarbons, hydrogen sulphide, phenol, benzene, toluene, xylene, nitrogen, ammonia, sulphur dioxide), and their airborne concentrations were shown to be well below the current limit values.
Moving: here, crude oil is pumped to the processing units, different commercial products denatured, gasoline ethylated, and all plant end-products moved by pumping to the storing and loading areas. No environmental measurements were available at the beginning of the study.
Delivery: workers in this department are in charge of all operations related to shipping commercial products, a job which implies mainly paper work and weighing operations. No environmental measurements were available.
Power plant: airborne concentrations of total hydrocarbons, sulphur hydrogen, sulphur dioxide, carbon monoxide and dioxide had been measured, and found to be below the current limit values.
Laboratories: they included analytical, chemical, physical and technological laboratories. No environmental measurements were available.
Maintenance: as usual, exposure of these workers is difficult to describe, since it might encompass any hazardous position in the plant.
Clerical: all employees in the personell and administration departments were included in this category.
Others: different units with limited numbers of workers and presumably very low or improbable exposure were grouped into this category.

Each individual work history was examined and for each worker the dates and periods of time spent in any of the categories recorded. The majority of the workers (62%) spent their entire in-plant career in one single category; 24% had only one change of category; the remaining 14% held jobs in more than two categories.

Workers' exposure classification was then attempted using three different criteria: having ever worked in that category; having had a job in that category as the longest job held during the working experience inside the plant; having worked in that category for the entire period of employment.

Vital status ascertainment. At the time the study was initiated, 806 employees were still active, while 789 had left the plant. Their vital status was ascertained as of December 31, 1982.

Information on vital statistics was obtained individually by contacting the Population Statistics Office of the municipality where the worker was residing at the closing date of the study. Several workers had moved from town to town after leaving the plant. In this case, the search started from the latest known residence while the worker was still employed, and hence through the different towns where the worker had moved, until the vital statistical information at the date of interest was reached. Death certificates reporting the underlying and contributory causes of death were obtained from these same sources, and death records were stored so as to ensure confidentiality. Causes of death were coded by nosologists trained by the National Statistics Institute of Italy (ISTAT), from which reference data were also drawn. The codes attributed were those of the international classification in use at the time deaths occurred, later converted to the VIII Revision, the one still in use in our country at the time the study was initiated.

Reference data. Mortality rates of the Italian population, 1946–1981, were available. However, marked inter-regional differences in mortality from several causes have been documented in our country. Thus, in order to deal with this problem [11], the mortality rates, 1951–1981, of a city of around 120000 inhabitants, having social and cultural characteristics similar to those of the area where our working population came from, were also adopted.

Analysis. For each person in the study, the period at risk was calculated from the date of entry into the plant to the date of death or end of study (whichever was earlier). The person-years contribution of each worker was calculated according to attained age (five-year classes), and calendar time of study (five-year periods). Person-years were similarly distributed according to length of employment and years since first employment. When considering year at first employment the entire contribution of person-years of each individual worker was attributed to the relevant category. Expected deaths were obtained by multiplying the cause, age, sex, and calendar time specific rates of the reference population times the corresponding number of person-years accrued by the study population. The comparison of mortality between the study and referent populations took the form of the ratio of observed-to-expected deaths, times 100 (standardized mortality ratio, SMR). Mortality was analyzed by length of employment, years since first employment, and year of first employment, always taking attained age and calendar period into account. Standardized mortality ratios by exposure category were also calculated; the categories were mutually exclusive when the classification criterion was 'longest job held' or 'always worked in that job', but obviously not so, when the criterion was 'ever worked'. In this analysis, the period at risk of each worker (and, hence, his person-years contribution) started at the date of entry in a certain exposure category. All these analyses were performed using a published and widely used computer program [48].

For the standardized mortality ratios the null hypothesis (Ho: SMR = 100) was tested, assuming a poisson distribution of the numerator, and the 95% confidence interval of the point estimate calculated according to the methods proposed by Miettinen, using the calculator programs made available by Rothman and Boice [32].

Table 1. Completion of the follow-up at the closing date of the study (December 31, 1982)

	No.	Percent
Workers in the study	1595	100.0
Alive	1363	85.4
Dead	213	13.4
Not traced	19	1.2

Table 2. Person-years of observation accrued during the study period (1949–1982), and their distribution by attained age and year of first employment

Attained age	Year of the first employment			Total
	< 1954	1954–1962	> 1962	
15–24	199.5	209.0	729.0	1137.5
25–34	2278.5	1230.0	3274.0	6782.5
35–44	4108.0	1870.0	2946.5	8924.5
45–54	4921.5	1412.0	893.5	7227.0
55–64	2872.0	671.5	154.0	3697.5
65–74	923.5	211.5	4.5	1139.5
≥ 75	91.5	42.0	0.0	133.5
Total	15394.5	5646.0	8001.5	29042.0

Results

The vital statistics were successfully ascertained for nearly 99% of the study subjects (Table 1). Two hundred thirteen deaths had occurred and 201 complete death certificates were obtained.

During the study period, nearly 30000 person-years of observation were accrued. Their distribution according to attained age and year of first employment is shown in Table 2.

In Table 3, results of the comparison of mortality from selected causes or group of causes in the study population with the corresponding mortality of the national and the local population are reported. In fact, quite different standardized mortality ratios were obtained depending upon the reference rates used. Overall mortality did not differ from the national one, while it was significantly lower than that of the local population. For each of the cancer causes considered, observed mortality was greater than expected from national rates with a few exceptions. The

Table 3. Mortality from selected causes among oil refinery workers in 1949–1982

Cause of death (ICD-8 codes)[a]	Observed deaths	National reference			Local reference		
		Expected deaths	SMR[b]	95% CI[c]	Expected deaths	SMR[b]	95% CI[c]
All causes (001–999)	213	207.71	102	89–117	267.02	80	69–91
All cancers (140–209)	79	53.10	149	118–185	80.58	98	78–122
Digestive system cancers (150–159)	23	18.45	125	79–187	26.86	86	54–128
Esophagus (150)	3	1.44	208	53–567	1.97	152	24–355
Stomach (151)	11	8.37	131	69–228	11.60	95	50–165
Large bowel (153)	2	2.81	71	12–235	3.38	59	10–195
Rectum (154)	3	1.69	177	45–483	2.47	121	31–330
Liver and gallbladder (155–156)	2	2.41	83	14–274	3.16	63	11–209
Pancreas (157)	2	1.78	112	19–371	2.93	68	14–225
Lung cancers (162)	29	14.54	199	136–283	23.80	122	82–175
Kidney cancers (189)	3	0.92	325	83–887	0.84	358	91–974
Brain tumors (191–192–225–238)	4	2.35	170	54–411	2.08	193	61–464
Lymphatic and hematopoietic cancers (200–209)	8	4.29	186	87–354	5.67	141	65–268
Lymphoma (200–202)	3	1.89	159	40–432	2.90	103	26–281
Leukemia (204–207)	5	1.90	264	96–583	2.03	246	90–544
All circulatory diseases (390–458)	65	74.12	88	68–112	94.83	68	53–87
Ischemic heart diseases (410–414)	36	33.61	107	75–148	48.47	74	52–103
Cerebrovascular diseases (430–438)	11	17.97	61	32–106	23.56	47	25–81
Respiratory diseases (460–519)	5	14.41	35	13–77	15.16	33	12–74
Digestive diseases (520–577)	13	20.93	62	34–103	25.81	50	28–84
Cirrhosis (571)	6	13.52	44	18–92	18.53	32	13–67
External causes (800–999)	18	22.20	81	50–126	20.51	88	57–136

[a] ICD-8 = International classification of diseases, eighth revision
[b] SMR = Standardized mortality ratio
[c] 95% CI = 95% Confidence interval

Table 4. Mortality from selected cancer causes of oil refinery workers according to length of employment in the plant; referent, local population

Cause of death		Length of employment (years)		
		<5	5–15	>15
All cancers	Obs/Exp	8/11.19	35/34.24	36/35.16
	SMR	72	102	102
Digestive system cancers	Obs/Exp	1/3.79	10/11.95	12/11.12
	SMR	26	84	108
Stomach	Obs/Exp	1/1.88	5/5.39	5/4.32
	SMR	53	93	116
Lung cancers	Obs/Exp	4/2.89	15/9.39	10/11.53
	SMR	139	160	87
Kidney cancers	Obs/Exp	0/0.14	2/0.33	1/0.37
	SMR	0	606[a]	270
Brain tumors	Obs/Exp	1/0.33	1/0.85	2/0.91
	SMR	303	118	220
Lymphatic and hemopoietic cancers	Obs/Exp	2/1.13	2/2.38	4/2.16
	SMR	177	84	185
Leukemia	Obs/Exp	1/0.45	1/0.92	3/0.67
	SMR	223	109	448[b]

[a]95% Confidence interval = 102–2002
[b]95% Confidence interval = 114–1219

Table 5. Mortality from selected cancer causes of oil refinery workers according to years elapsed since the beginning of employment; referent, local population

Cause of death		Years since first employment		
		<10	10–20	>20
All cancers	Obs/Exp	9/12.24	30/26.91	40/41.45
	SMR	74	111	96
Digestive system cancers	Obs/Exp	1/4.23	12/9.68	10/12.94
	SMR	24	124	77
Stomach	Obs/Exp	1/2.50	7/4.29	3/4.80
	SMR	40	163	62
Lung cancers	Obs/Exp	3/3.03	9/7.28	17/13.49
	SMR	99	163	62
Kidney cancers	Obs/Exp	0/0.12	1/0.20	2/0.52
	SMR	0	500	385
Brain tumors	Obs/Exp	2/0.42	2/0.78	0/0.88
	SMR	479	256	0
Lymphatic and hemopoietic cancers	Obs/Exp	2/1.42	4/1.82	2/2.43
	SMR	141	220	82
Leukemia	Obs/Exp	1/0.59	3/0.64	1/0.82
	SMR	171	469[a]	122

[a]95% Confidence interval = 119–1276

Table 6. Mortality from selected cancer causes of oil refinery workers according to calendar period of first employment; referent, local population

Cause of death		Calendar period of first employment		
		<1954	1954–1962	>1962
All cancers	Obs/Exp	60/58.64	14/15.57	5/6.37
	SMR	102	90	78
Digestive system cancers	Obs/Exp	17/20.04	5/5.11	1/1.71
	SMR	85	98	58
Stomach	Obs/Exp	8/8.85	3/2.15	0/0.60
	SMR	90	139	0
Lung cancers	Obs/Exp	24/16.93	5/4.61	0/2.26
	SMR	142	108	0
Kidney cancers	Obs/Exp	2/0.63	1/0.17	0/0.04
	SMR	318	604	0
Brain tumors	Obs/Exp	3/1.45	0/0.40	1/0.22
	SMR	206	0	454
Lymphatic and hemopoietic cancers	Obs/Exp	3/3.81	2/1.14	3/0.72
	SMR	79	175	417[a]
Leukemia	Obs/Exp	1/1.24	1/0.41	3/0.40
	SMR	80	245	750[b]

[a]95% Confidence interval = 106–1134
[b]95% Confidence interval = 191–2041

noted excesses turned out to be statistically significant for all cancers and lung cancer, and close to significant for deaths due to leukemias. In comparison with the local rates, for no cancer sites did the SMR depart significantly from 100. Deaths from cancer of the esophagus, rectum, lung, and lymphopoietic neoplasms were slightly higher than expected. More pronounced, albeit statistically not significant, was the excess mortality from kidney cancer, brain tumors, and leukemias. Among malignancies, the only instances in which the SMRs were higher when based on local, rather than national expected figures were kidney cancer and brain tumors. One single case of melanoma and one of prostate cancer were observed.

The numbers of observed deaths from non-malignant diseases were consistently lower than expected. The only exception was ischemic heart disease, when compared with national rates. In particular, the large deficits in mortality from non-malignant respiratory diseases, diseases of the digestive system, and cirrhosis were noteworthy.

In the following tables, only comparison with local rates will be reported, the one considered the most appropriate in the light of the previously mentioned inter-regional variations in cancer mortality.

Table 7. Mortality from selected cancer causes of oil refinery workers according to the department in which they had ver worked; referent, local population

Cause of death		Exposure classification by department (ever worked)							
		Production	Delivery	Moving	Maintenance	Power plant	Laboratories	Clerical	Others
All cancers	O/E	19/21.50	13/5.61	22/11.68	16/18.10	11/6.96	5/5.26	15/21.00	13/17.99
	SMR	88	232[a]	188[b]	88	158	95	71	72
Digestive system cancers	O/E	6/6.73	4/1.89	4/3.74	6/6.00	2/2.29	1/1.63	5/7.30	2/6.04
	SMR	89	212	107	100	88	61	69	33
Stomach	O/E	4/2.73	1/0.78	1/1.59	3/2.55	2/0.98	1/0.63	1/3.22	1/2.57
	SMR	147	127	63	118	204	158	31	39
Lung cancers	O/E	5/6.80	3/1.67	11/3.61	3/5.44	6/2.11	2/1.65	6/5.96	7/5.31
	SMR	73	179	305[c]	55	285[f]	121	101	132
Kidney cancers	O/E	0/0.20	0/0.06	0/0.12	2/0.18	0/0.07	0/0.05	0/0.24	1/0.20
	SMR	0	0	0	1112[e]	0	0	0	501
Brain tumors	O/E	2/0.65	1/0.14	3/0.33	1/0.46	1/0.19	1/0.17	0/0.47	0/0.44
	SMR	307	695	900[d]	219	540	573	0	0
Lymphatic and hemopoietic cancers	O/E	2/1.66	0/0.36	0/0.85	1/1.25	0/0.48	1/0.40	2/1.32	2/1.19
	SMR	121	0	0	80	0	247	152	169
Leukemia	O/E	2/0.61	0/0.11	0/0.30	1/0.43	0/0.16	0/0.13	1/0.45	1/0.42
	SMR	330	0	0	232	0	0	222	238

[a] 95% Confidence interval = 129–386
[b] 95% Confidence interval = 118–285
[c] 95% Confidence interval = 160–530
[d] 95% Confidence interval = 229–3000
[e] 95% Confidence interval = 186–3675
[f] 95% Confidence interval = 115–592

Analysis by length of employment yielded the results reported in Table 4. No definite patterns or clear-cut increasing trends in mortality were discernible, with the possible exception of digestive and stomach cancer. Three leukemia deaths in the category of longest exposure made up a four-fold, statistically significant excess. Also significant was the increased SMR for kidney cancer among those in the 5 to 15 year category; only two deaths, however, were observed.

Analysis by years since first employment failed to show consistent patterns in mortality (Table 5). The largest excesses were seen, in general, after 10 to 20 years since starting work in the plant. The departure from 100 of the SMR for leukemia in this subcohort was statistically significant.

The calendar time of first employment appeared to be somehow associated with the mortality experience of the employees. Intervals were chosen, on an a priori basis, so as to correspond to periods of major changes in the production history of the plant. As shown in Table 6, the lung cancer excess, although statistically nonsignificant, was confined to those first employed in the early period of operation, prior to 1954. Three of the four brain tumors and two of the three kidney cancer deaths had occurred in this same subcohort of workers, making up respectively a two-fold and three-fold statistically not significant excess mortality. The increased mortality from lymphopoietic neoplasms reached statistical significance among those first employed after 1962, and was entirely due to leukemia deaths.

As regards cancer mortality by exposure category, workers were first classified as having ever worked in any of the categories (Table 7). Consequently, some of them are included in more than one category, and their deaths are counted more than once (total = 287 deaths, instead of 213). In Production, none of the SMR was significantly different from 100, although suggestions of increased mortality from stomach cancer and, particularly, leukemias and brain tumors were noted. Mortality from all cancers among workers ever employed in Delivery was significantly elevated. No clusters of cancer deaths at specific sites departing significantly from expectations were seen; yet, mortality from cancer of the digestive tract and

Table 8. Mortality from selected cancer causes of oil refinery workers having always operated in a single dpartment; referent, local population

Cause of death		Exposure classification by department (unique job)							
		Production	Delivery	Moving	Maintenance	Power plant	Laboratories	Clerical	Others
All cancers	O/E	7/8.57	1/0.91	9/4.40	12/11.35	4/3.18	3/1.81	9/13.98	7/9.84
	SMR	82	109	204[b]	106	126	166	64	71
Digestive system cancers	O/E	3/2.66	1/0.32	3/1.46	4/3.83	2/1.10	1/0.53	3/5.02	0/3.43
	SMR	113	314	206	105	181	188	60	0
Stomach	O/E	2/1.09	1/0.15	1/0.65	2/1.66	2/0.50	1/0.20	0/2.30	0/1.52
	SMR	184	674	155	120	399	492	0	0
Lung cancers	O/E	0/2.71	0/0.25	4/1.30	3/3.36	1/0.92	1/0.59	3/3.80	4/2.73
	SMR	0	0	309	89	109	169	79	147
Kidney cancers	O/E	0/0.08	0/0.01	0/0.05	2/0.11	0/0.04	0/0.02	0/0.17	1/0.12
	SMR	0	0	0	1750[c]	0	0	0	838
Brain tumors	O/E	0/0.26	0/0.02	0/0.12	0/0.27	1/0.06	0/0.06	0/0.28	0/0.22
	SMR	0	0	0	0	1632	0	0	0
Lymphatic and hemopoietic cancers	O/E	2/0.71	0/0.07	0/0.32	1/0.77	0/0.21	1/0.15	2/0.87	2/0.64
	SMR	282	0	0	129	0	675	231	314
Leukemia	O/E	2/0.28	0/0.02	0/0.11	1/0.28	0/0.08	0/0.05	1/0.32	1/0.24
	SMR	704[a]	0	0	362	0	0	314	417

[a] 95% Confidence interval = 118–2327
[b] 95% Confidence interval = 100–375
[c] 95% Confidence interval = 293–5781

lung was clearly elevated. Among workers in Moving, statistically significant increases were noted for all cancers and cancer of the lung, based on 22 and 11 deaths, respectively; also significant was the elevated mortality from brain tumors. Indications of an unusual mortality experience from kidney cancer emerged among Maintenance workers; only two deaths were observed, but they made up a significant increase above expectations. Workers in Power Plant exhibited a higher than expected mortality from cancer causes; the excess of lung cancer deaths reached statistical significance. In the Laboratories few deaths were observed. Among Clerical workers the only SMR above 100 was noted for lymphopoietic neoplasm deaths. Workers classified as Others exhibited a number of deaths due to lung cancer and lymphopoietic neoplasm slightly higher than expected.

Analysis by job held longest tended to confirm the previous findings; of course, smaller numbers affected statistical significance.

Table 8 presents results of analysis for those workers always employed in one single department. The two leukemia deaths among Production workers yielded an SMR of around 700, statistically significant. The increase in all cancer mortality among moving operators was of borderline significance; the previously noted three-fold increased lung cancer risk remained essentially unchanged. The elevated risk from kidney cancer among Maintenance workers was confirmed.

Lung cancer mortality among moving operators was further analyzed in order to control for possible confounding by smoking. The plant health service had been recording the smoking habits of the workers, as reported by workers themselves at the time of hiring. Unfortunately, not all the records had been kept and thus at the time the study was conducted, the smoking habits were known for more than 95.0% of the active workers, but only for 10.4% of former employees. The proportional distribution of these retired workers by exposure category turned out to be almost identical to that of current employees, thus suggesting that this sample was not heavily biased, and probably representative of the smoking habits of the past workforce. We thought it reasonable, then, to base the estimate of the smoking habits in the entire cohort upon this information, even though it was limited. The percentage of habitual smokers in each exposure category turned out to be as follows: Production 71%, Delivery 67%, Moving 70%, Mainte-

Table 9. Hypothetical smoking adjusted SMRs for lung cancer among Moving operators (unadjusted SMR = 305), and smoking distribution in the referent population to be assumed to sustained the hypotheses

Adjusted SMR	Smoking distribution in the referent population (cigarettes/d)			
	Non-smokers	< 10	10–20	> 20
100	> 75%	< 20%	< 5%	0%
150	> 45%	5–50%	< 25%	< 5%
200	> 20%	5–75%	< 35%	< 15%

nance 60%, Power plant 60%, Labs 67%, Clerical 73%, Others 56%. Based on these data, it seemed quite hard to interpret the outstanding excess of lung cancer deaths noted among Moving operators on the sole basis of smoking habits. The method suggested by Axelson in order to control for smoking [5] was adapted to our data. The distribution of smoking habits among the workers was estimated from the available data. Estimates of the lung cancer relative risk associated with different smoking habits were assumed to be 5.0 for smoking < 10 cigarettes/d, 10.0 for 10 to 20 cigarettes/d, and 20.0 for > 20 cigarettes/d. We then calculated the smoking habit distribution in the referent population necessary to explain the three-fold increase in lung cancer mortality noted among these workers solely on the basis of differences in smoking habits between the study and referent population, viz. true SMR after controlling for smoking = 100. This distribution is shown in Table 9, and appeared too extreme to be credible. The table gives a more general view of the extent of confounding possibly introduced by smoking in these results. Only a smoking adjusted SMR = 200 (or greater) appeared to possibly correspond to reasonably anticipatable smoking distributions in the referent population.

Discussion

This cohort of Italian oil refinery workers had a cancer mortality significantly higher than expected from the population of the same sex and birth cohort in the whole country. The excess mortality was noteworthy for several causes, which corresponded well to those suggested by previous studies, i.e. lung (the elevated SMR being statistically significant), digestive tract, kidney, lymphatic and hemopoietic tissues and brain. Quite a different pattern was obtained when local death rates were used to calculate expected numbers. Yet, despite the dramatic decrease of nearly all SMR values, the excess mortality from kidney cancer, brain tumors and leukemias remained essentially unchanged.

Under the assumption that an association between workers' mortality and working experience exists, one expects that the longer the employment, the more pronounced the effect will be. Exception to that are short-term employees, whose mortality usually appears to be unfavourable [12]. Suggestive increases in mortality with increasing length of employment were only noted for cancer of the digestive tract.

The time elapsed since the beginning of employment is not only a popular, but also a viable approximation of the time required for a long-term effect (e.g. cancer) of chemical exposure to become manifest [31]. In our data, however, no clear indications of an increased risk with increasing number of years since first employment emerged.

The calendar period in which employment started is of interest for several reasons. For instance, it is reasonable to assume that in early periods working conditions were poorer, owing to both the type of technology in use and the quality and extent of protective devices available. In addition, such an analysis may help in pinpointing periods of the production history involving particular risks. It was thus noted that the slight increase of lung cancer mortality noted in the entire cohort was clearly related to early years of employment. This was also the case for kidney cancer and brain tumors. The statistically significantly elevated risk from neoplasms of lymphatic and hemopoietic tissues, and more specifically leukemias, noted for those first employed after 1962, could not be associated, to the best of our knowledge, to peculiar exposure opportunities inside the plant during such a time period.

Thus, results for the entire cohort of refinery workers provided suggestions of a possibly unusual mortality owing to leukemias, kidney cancer, brain tumors and lung cancer in some segments of the cohort.

Analysis according to job held inside the plant shed some further light. The increased risk from leukemias appeared to be associated with working in production. Interpretation of the nature of this association was hampered by the small number of deaths observed. Exposure to hydrocarbons (including benzene) in recent years was shown to be well below the current limit values. Measurements in the past years were not available, yet the assumption that concentrations in the past were higher is most reasonable. The two workers always employed in production who died from leukemia (one "acute leukemia" and one chronic lymphatic leukemia) started work in the early 1950s, and their exposure lasted for more than 15 years. An increased risk from leukemias had been suggested by previous investigations [10, 24, 37, 40, 41, 45]. In one study a statistically significant increase was found; the excess mortality was mainly due to acute myeloid leukemia [24], and it was not possible to relate this excess to any particular job or department, or specifically to benzene exposure [4]. In another one [41], the increase was related to working in Treating (a job title similar to our production), and Boiler-making (included in our maintenance). The latter job was also found at risk in another study [10].

The most distinctive pattern of increased cancer mortality seemed to be the one observed in association with moving operations. Significant excess mortality from all cancers, lung cancer and brain tumors was noted. Analysis by longest job held, and always in that job, confirmed, despite obvious numerical changes, the findings for all cancers and lung cancer, but did not allow attributing the increased brain tumor risk specifically to working in this department. The four lung cancer cases always employed in this department, all started work before 1955, and had a minimum length of exposure of 15 years. Exposure was composite, given the numerous operations performed, and possibly included, other than various hydrocarbons, hydrogen sulphide, tetraethyl lead, and several substances employed for denaturing commercial products; denaturing agents included, among others, dyes (in liquid and sometimes powder state), furfurole, diphenylamine, phtalates. All operations were automated. However, tanks of denaturing substances were sometimes filled up manually and samples taken manually for quality control purposes. The greatest opportunity for exposure to volatile hydrocarbons occurred during the loading operations, which required the manual connection of oil filler pipes to truck and train tanks, and manual measurements of product levels in tanks. In addition, workers were exposed, while staying at the filling platform, especially during the hot season, to volatiles coming from open tanks of standing trucks and trains. No measurements were available, as already stated, at the beginning of the study. They were taken, however, in 1985 and documented that a potential for high exposure actually existed. This, in fact, turned out to be the only department inside the plant where values higher than the current threshold limit values (TLV) were measured. Thus, for instance, at the "super gas oil" platform, during the manual sampling of filled tanks, five samples of total hydrocarbons showed values between 230 and 419 mg/m^3, vs a TLV of 180 mg/m^3; two samples taken by means of personal passive sampler had values of 223 and 851 mg/m^3. Potential exposure to polynuclear aromatic hydrocarbons (PAHs) also existed during manual loading of packed bitumen. Thus, the excess lung cancer mortality noted among employees in this department might assume credibility in the light of the environmental findings. An association of lung cancer mortality with working in the petroleum industry was first suggested by mortality investigations in the general population [13, 28] and ecological studies [6, 7]. Further studies gave contrasting results. Two of them showed significantly elevated risks for lung cancer [14, 39], but could not associate that increase with occupations involving specific exposures. Five studies, on the other hand, found relative risks lower than 1.00 [15, 33, 37, 45, 47].

Oil refinery workers have been shown to smoke less than workers in other industries [42]. We had no data from our country to corroborate those findings. However, smoking could be excluded as sufficient explanation for the increased lung cancer risk noted in this exposure category, for several reasons. First, internal comparison among exposure categories showed that the pattern of the estimated frequency of smokers could not represent a satisfactory explanation for the results. Second, it was shown that for smoking to be the explanation of the three-fold increased lung cancer risk, it was necessary to assume a distribution of smoking habits in the reference population clearly not credible. Third, mortality from causes other than cancer known to be associated with smoking was definitely lower than expected; so, for example, five deaths from cardiovascular diseases were observed among moving workers vs 12.5 expected, and no deaths from chronic respiratory diseases were found vs 1.9 expected.

The increased mortality from all cancers suggestively associated with working in delivery might also find a possible explanation in the sort of exposure just described for moving. As a matter of fact, workers in delivery had the potential for exposure to the same type of chemicals as the movers, especially during weighing operations.

The excess lung cancer mortality noted among power plant workers almost disappeared when analysis was restricted to those always employed in the department. Still, the type of exposure, and the concentrations being possibly much higher in the past, renders this finding noteworthy too.

The possible link between petroleum hydrocarbons and renal damage has been extensively reviewed recently [27], and a possibly elevated kidney cancer risk was suggested [15, 25, 26, 40, 46]. In our study, having always worked in maintenance appeared to carry an increased risk from kidney cancer in comparison with the local population. Apart from statistical significance, the small number of deaths observed prevented firmer conclusions. The suggested increase can be hardly associated with any specific exposure because of the very nature of maintenance jobs. The two workers deceased from kidney cancer had been both exposed for more than ten years, in the early period of operations (< 1954), and died 10 and 22 years after first exposure.

The increased mortality from brain tumors, which was noteworthy in the whole cohort, could not be linked to any specific job or working process. The association of such an increased risk with oil refining had been suggested by numerous studies [2, 10, 15, 29, 37, 38, 40]. None, however, could conclusively establish a causal link.

On the basis of these findings, we thought that a further study of workers engaged in operations such as pumping and moving of petroleum products, and allied operations (e.g. marketing and distribution) was likely to be the most motivated and rewarding. Accordingly, we are collecting a larger cohort of similar workers from other plants and distribution centers, in order to further explore the cancer risk, if any, actually carried by exposures occurring during such operations. Concurrently, extension in time of the follow-up for the entire cohort has been planned.

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