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impact on the health of the population.
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Industrial Activities in Sites at High Environmental Risk and Their Impact on the Health of the Population

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A second mortality analysis of 15 areas of Italy identified in 1986 by the Italian Ministry of Environment as areas at high risk of environmental crisis has confirmed and extended the findings of the first. In regional comparisons, these areas, in which potentially hazardous industries are located, show excesses of deaths from almost all cancers and other diseases, particularly among men. Although more information is needed to identify corrective public health measures, the official recognition of areas in need of cleaning up, which appears to be unique to Italy and which fostered the study, is a promising beginning. *Key words*: public health; mortality studies; epidemiology; environmental risk areas; Italy.

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In 1986 the Italian Ministry of Environment identified 15 areas, widely distributed throughout the country, as at "high risk of environmental crisis" (Figure 1). These areas (thereafter referred to as "risk areas") host large industrial activities that may entail noxious exposures, through occupation and the general environment. In some of them, hazardous chemical accidents have occurred in the past. Risk areas are heterogeneous with respect to number and size of municipalities, demographic and geographic dimensions, occupational and environmental exposures, socioeconomic profiles, productive structures, cultural backgrounds, and degrees of urbanization.

Besides environmental degradation, one of the main concerns was the possible adverse effects on the health of the populations living and working in the risk areas. The Ministry of Environment requested WHO, European Center for Environment and Health, to carry out an epidemiologic investigation into such health implications. A first report, covering the period 1980–87, was

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published.¹ Mortality was excessive and evidence of environmental damage was documented. Following this first mortality study and given the continuing concern expressed by residents, local authorities, workers, and unions, further analyses were planned in order to update and develop the descriptive epidemiologic information on the risk areas. Thus a second, more indepth investigation, covering the period 1981–94, was conducted,² applying a wider range of epidemiologic methods for small-area studies, including disease mapping, time-trend analyses, cohort effects, and investigation of socioeconomic factors.

It was the first time that, in Italy, this environmental and health issue was addressed and analyzed with descriptive epidemiologic studies not only at a local level, but in different parts of the country in a systematic way. These studies aimed to provide government as well as local administrators with elements for the description and understanding of the health status of the populations living in the risk areas and to indicate priorities for future corrective public health actions.



Figure 1—Areas at high risk of environmental crisis in Italy. ■ Risk areas presented in this paper.

TABLE 1 Areas at High Risk of Environmental Crisis

	Area Population (1991)	Number of Municipalities	Reference Population in the Analyses	Area Pop./ Reference Pop. (%)	Main Environmental Risk Factors
Massa Carrara	132, 931	2	Region	3.8	Mix of industrial activities, marlbe industry, chemical plant
Manfredonia	97,210	3	Province	2.4	Petrochemical plant, accident with arsenic release
Brindisi	130,298	4	Region	3.2	Shipbuilding industry, petrochemical plant, power plants
Taranto	279,141	4	Region	6.9	Iron and steel industry, shipbuilding industry
Portoscuso	54,616	5	Province	3.3	Mines, metallurgy industry, thermo- electric power plant
Augusta-Priolo	209,371	6	Region	4.2	Petrochemical plant, shipbuilding industry
Gela	104,876	3	Region	2.1	Petrochemical plant

MATERIALS AND METHODS

In this paper, descriptive results for seven of the 15 areas are synthetically reported (Table 1). These are small areas, including some 1 million residents, and were selected as they share the presence on their territories of few and localized industrial facilities, rather than widespread sources of pollutants as in larger, more complex areas.

Population, sociodemographic, and mortality data at the level of municipality from 1981 to 1994 were retrieved from the ISTAT (the National Bureau of Statistics) database. About 30 causes of death, including most major groups of non-cancer causes, major cancer sites, and several subgroups and rare diseases, were selected to explore a wide range of possible health effects (Table 2).

Since only mortality data were systematically available in Italy at the time of the analysis, extensive statistical and epidemiologic analyses of mortality were carried out. Most analyses were conducted separately for men and women. For each risk area some analyses were done using all its municipalities combined and other analyses were based on data from separate municipalities. In the former, numbers of deaths, crude rates, standardized mortality rates, standardized mortality ratios (SMRs) with regional (or provincial) reference, deaths for "stable" population (the population dead in the province of birth or in an adjacent province) and proportional standardized mortality ratios (SPMRs), and cumulative risk of dying before 65 years of age were calculated for the period 1990-94. Possible socioeconomic confounding was controlled using a deprivation index³ built at municipality level with five census variables based on education, unemployment, housing quality and family structure; SMRs standardized by age and deprivation index (SMRs+DI) were also calculated. 95% confidence intervals (CIs) were computed.

Regression models were applied to investigate time trends over three periods (1981–84, 1985–89, 1990–94)

TABLE 2 Causes of Death

	ICD IX code
All-causes mortality	0–999
Non-tumoral causes Diseases of the circulatory system Infarction, angina pectoris, and ischemic heart diseases Cerebrovascular diseases Diseases of the respiratory system Chronic respiratory system disease Diseases of the digestive system Chronic liver disease and cirrhosis Diseases of the genitourinary systel Infectious and parasitive diseases Diabetes mellitus Symptoms, signs, and ill-defined conditions Mental disorders Injury and poisoning	520-579 571
Tumoral causes All cancers Malignant neoplasm of stomach Malignant neoplasm of colon Malignant neoplasm of liver and bile ducts Malignant neoplasm of larynx Malignant neoplasm of trachea, bronchus, and lung Malignant neoplasm of pleura Malignant neoplasm of bladder Malignant neoplasm of central nervous system Lymphohematopoietic system Non-Hodgkin's lymphoma Hodgkin's disease Multiple myeloma Leukemias Malignant neoplasms of bone and soft tissues Malignant melanoma of skin Malignant neoplasm of uterus Malignant neoplasm of prostate Malignant neoplasm of female bre Malignant neoplasm of testis Malignant neoplasm of testis	140-239 151 153-154 155.0-155.1, 156 161 162 163 188 191-192, 225 200-208 200, 202 201 203 204-208 170-171 172 179-180, 182 185 east 174 186 183

TABLE 3 All-causes Mortality in Areas at High Risk of Environmental Crisis SMRs and SMRs standardized by Deprivation Index (DI), 1990–94

	Cases		Men		Women		Men		Women	
	Men	Women	SMR	95% CI	SMR	95% CI	SMR+DI	95% CI	SMR+DI	95% CI
Gela	2,086	1,735	103.6	99.2-108.1	113.7	108.5-119.2	109.2	104.6-113.9	117.4	112–123
Augusta-Priolo	4,118	3,634	99.2	96.2-102.3	95.6	92.5-98.8	105.3	102.1-108.5	99.1	95.9-102.4
Portoscuso	1,365	959	105.5	100-111.2	97.3	91.3-103.6	98.5	93.4-103.8	95.2	89.4-101.4
Brindisi	2,515	2,118	107.2	103.1-111.5	97.2	93.1-101.4	105.2	101.2-109.4	95.9	91.9-100
Taranto	5,572	4,694	110.6	107.7-113.5	103.8	100.9-106.8	107.4	104.6-110.2	101.6	98.8-104.6
Manfredonia	1,696	1,498	92.0	87.7-96.5	88.8	84.4-93.4	95.4	91-100	90.9	86.4-95.6
Massa Carrara	3,741	3,500	119.8	116-123.7	105.0	101.6-108.5	115.3	111.7–119.1	104.2	100.8-107.7

TABLE 4 All-cancer Mortality in Areas at High Risk of Environmental Crisis SMRs and SMRs standardized by Deprivation Index (DI), 1990–94

	Cases		Men		Women		Men		Women	
	Men	Women	SMR	95% CI	SMR	95% CI	SMR+DI	95% CI	SMR+DI	95% CI
Gela	473	278	95.8	87.5–104.8	86.8	77.2–97.7	104.3	95.3–114.1	91.3	81.2–102.7
Augusta-Priolo	1,127	767	110.1	103.9-116.7	102.3	95.3-109.8	122.2	115.3-129.6	109.2	101.7-117.2
Portoscuso	371	234	100.2	90.5-110.9	97.4	85.8-110.8	93.0	84-102.9	91.5	80.5-103.9
Brindisi	777	474	113.6	105.9-121.9	101.3	92.6-110.8	112.2	104.6-120.4	100.8	92.1-110.3
Taranto	1,644	1,064	111.7	106.4-117.2	107.2	100.9-113.8	108.7	103.6-114.1	105.7	99.6-112.3
Manfredonia	445	329	93.3	85-102.4	97.5	87.6-108.8	96.7	88.1-106.1	96.6	86.7-107.6
Massa Carrara	1,300	786	119.7	113.4-126.4	93.5	87.2-100.2	113.2	107.2-119.6	90.7	84.5-97.2

for SMRs; trends for standardized mortality rates were also analyzed. Cumulative risks of dying until 65 years of age were estimated for the generations born in the quinquennium 1920, 1925, 1930, 1935, and 1940 through an age-cohort regression model; bootstrap iterative techniques⁴ were applied to compute 95% uncertainty intervals.

Municipality-specific data were also used for withinarea analyses. Analysis of spatial heterogeneity of mortality (1990–94) among municipalities was carried out using a gamma-Poisson model⁵ in an approximately circular region centered in each risk area. The distribution of risks in the municipalities inside the risk area was compared with that in the surrounding region, and homogeneity of risks in the circular region was statistically tested. SMRs and empirical Bayesian estimators (EBRs)⁶ were mapped at the level of municipality to identify local excess of risk after removing random fluctuations.

Results from area-specific analyses were used to characterize the mortality profile of the set of the risk areas combined. Even though it is difficult to identify common risk factors for all the risk areas, due to their specificities, such syntheses can help provide an indication of the order of magnitude of the likely excesses (or deficits) of mortality in the risk areas. In order to do that, SMRs were tabulated for all areas combined by cause of death and for all causes combined by area. Results are shown for both sexes combined. In addition to that, the differences between the numbers of observed and expected cases by sex, for all the causes of death and for all the areas, were calculated. For each cause of death these values were calculated by the algebraic sum of mor-

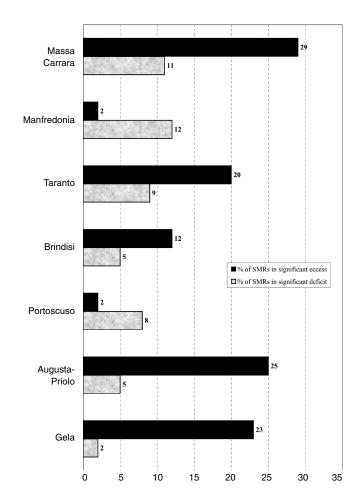


Figure 2—SMRs standardized by DI combined for all causes of death by area.

all causes circulatory system infarction cerebrovascular Non tumoral causes respiratory system chronic respiratory digestive system cirrhosis genitourinary infectious diabetes ill defined mental disorders injury and poisoning all cancers Tumoral causes prostate uterus stomach colon liver and bile ducts larynx lung pleura bladder central nervous system lymphoem system ■ % of SMRs in significant eccess non-Hodgkin ■% of SMRs in significant deficit Hodakin disease multiple mieloma leukemia female breast bone and STS melanoma of skin testis ovary 0 10 20 30 40 50 60

Figure 3—SMRs standardized by all areas and both sexes combined by cause of death.

tality excesses and deficits, only considering the areas in which SMRs were significantly different from 100.

RESULTS

All-cause mortality and all-cancer mortality in the selected risk areas, with number of cases, SMRs (adjusted and not adjusted for deprivation), and 95% CIs, separately for men and women, are reported in Table 3 and Table 4. In both tables several areas have risks in significant excess compared with the expected values based on reference region. The standardization by DI in several cases substantially changes the risk estimates, which suggests an important role of socioeconomic factors in confounding the association between residence in the areas and mortality.

The analysis for all areas combined by cause of death involves a large number of statistical tests, one for each SMR calculated. On the basis of random variability alone, around 2.5% of excesses and 2.5% of deficits are expected. However the proportions of significant mortality excesses and deficits differ substantially (Figure 2). For instance, in the case of Augusta-Priolo, 25% of excesses and only 5% of deficits are observed and, with only two exceptions (Manfredonia and Portoscuso), this is a common pattern for the five remaining areas.

Similarly, a prevalence of excesses, compared with deficits, is evident in the analyses of each cause of death for all areas and both sexes combined (Figure 3). In 50% of the analyses, all-cause mortality is higher than the regional average; similar values can be observed for all cancers and lung cancer (36%), digestive diseases and cirrhosis (43%), respiratory disease (29%), and pleural cancer (21%).

The algebraic sum of mortality excesses and deficits for each cause of death confirms that the mortality profile of the population living in the risk areas is critical compared with the surrounding regions (Table 5). 1,459 deaths in excess (about 292 per year, mostly occurring in men (1,303, or 261 per year; for women 155, 31 per year) were observed in the period 1990-94. Several excesses were observed: in men, in respiratory (225 deaths in excess) and digestive diseases (169), cirrhosis (154), and lung cancer (326), which explains the

TABLE 5 Deaths in Significant Excess and Deficits for All Areas by Cause of Death

All Causes of Death	Men	Women	Total
Non-tumoral causes			
All causes mortality	1,303	155	1,459
Diseases of the circulatory system	-112	-396	-508
Infarction, angina pectoris, and ischemic heart disease	233	-9	224
Cerebrovascular diseases	44	39	83
Diseases of the respiratory system	225	99	324
Chronic respiratory system diseases	90	30	120
Diseases of the digestive system	169	113	282
Chronic liver disease and cirrhosis	154	118	272
Diseases of the genitourinary system	0	0	0
Infectious and parasitive diseases	0	0	0
Diabetes mellitus	0	88	88
Symptoms, signs, and ill-defined conditions	79	74	153
Mental disorders	13	25	38
Injury and poisoning	114	6	121
Tumoral causes			
All cancers	574	-16	557
Malignant neoplasm of stomach	40	_0	40
Malignant neoplasm of colon	0	17	17
Malignant neoplasm of liver and bile ducts	7	0	7
Malignant neoplasm of larynx	-18	0	-18
Malignant neoplasms of trachea, bronchus, and lung	326	0	326
Malignant neoplasm of pleura	37	3	40
Malignant neoplasm of bladder	38	-7	31
Malignant neoplasm of central nervous system	-7	0	-7
Lympho-hematopoietic system	16	-33	-17
Non-Hodgkin's lymphoma	11	-4	7
Hodgkin's disease	0	0	0
Multiple myeloma	0	0	0
Leukemias	0	-15	-15
Malignant neoplasms of bone and soft tissues	0	-3	-3
Malignant melanoma of skin	11	0	11
Malignant neoplasm of uterus	20	13	13
Malignant neoplasm of prostate	30	00	30
Malignant neoplasm of female breast	^	28	28
Malignant neoplasm of testis	0	10	0
Malignant neoplasm of ovary		-12	-12

main part of 574 deaths in excess for all the cancers; in women, large excesses can be observed in cirrhosis (118) and digestive diseases (113). Deficits were observed for both sexes for only the total diseases of circulatory system (508 deaths in deficit), but not for infarction and cerebrovascular diseases.

Figures 4–6 illustrate the use of the methods described above for spatial and time-trend analyses. In the risk area of Taranto (Figure 4) interesting time trends for all-cancer causes for men can be observed. Mortality levels are always higher than regional averages for the three observed periods, even though the trend for SMRs is declining and statistically significant (p = 0.002). At the same time, all-cancer mortality, in absolute terms, is increasing. This suggests that, in the 15 years analyzed, the health status of the Taranto male population has been worsening in absolute terms, but it has been improving if compared with the regional situation. An example of analysis of birth-cohort effects is presented for the risk area of Augusta–Priolo (Figure 5). Malignant neoplasms of the trachea, bronchus, and

lung for men are analyzed. In a general scenario of declining overall mortality, cumulative risks for the 1940 generation almost double, if compared with the 1920 generation risks (from 3.35 to 6.58). The asymmetric uncertainty intervals are due to the use of bootstrap iterative technique.

In the risk area of Brindisi (Figure 6), non-Hodgkin's lymphomas for both sexes are mapped. It can be seen from the SMRs maps that similar situations of high risk exist for men and women. But, after EBRs are calculated and mapped, the risk estimates are more stable and not affected by random fluctuation only for men, while for women there is a situation of "flat" risk. This observation is confirmed by the results of the test for spatial heterogeneity (p < 0.01 for men and not statistically significant for women).

CONCLUSIONS

As in the first report on the environment and health in Italy,¹ the analyses confirm substantial excesses in mor-

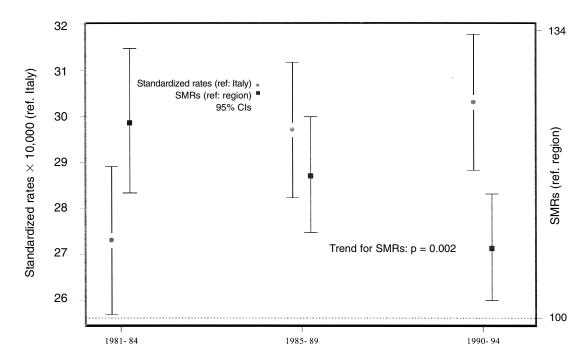


Figure 4—Area of Taranto: all cancers, men.

tality for residents in risk areas. This applies both to individual areas and to the seven risk areas combined together. The same kind of combined analyses gave a similar indication for the entire set of risk areas.² Unfortunately, we are not aware of similar published studies in national and international scientific literature.

It is difficult to explain these excesses, since risk areas are characterized by a heterogeneous set of risk factors (and protective factors) which can influence the mortality profile and health status in different ways, and whose effects are difficult to distinguish. In addition to that, the lack of further health data limits the analysis to mortality, the only health information that is systematically available in Italy with national coverage. The availability of systematic and detailed data on morbidity, adverse reproductive outcomes, hospital admis-

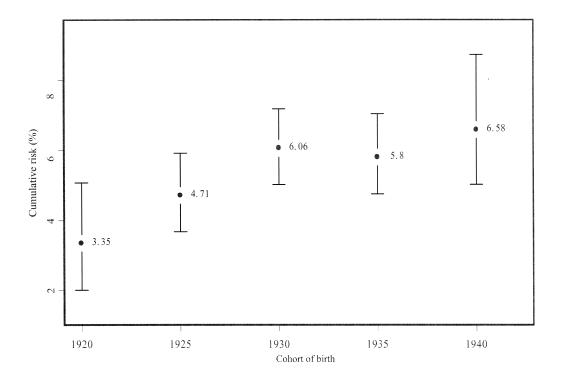
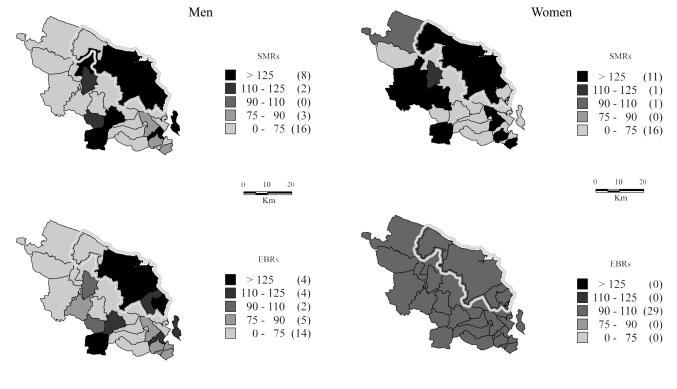
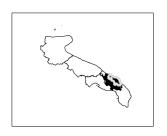


Figure 5—Area of Augusta–Priolo: malignant neoplasms of the trachea, bronchus, and lung, men.



Men: 90% of relative risks between 21 and 228 Homogeneity test: p < 0.01

Figure 6—Area of Brindisi (four municipalities), non-Hodgkin's lymphoma, 1990–94. Risk estimates calculated for 29 municipalities; reference population identified by a 37-km radius circle centered in Brindisi.



Women: 90% of relative risks between 93 and 107 Homogeneity test: p = ns

sions, medical visits, and use of medicine could allow evaluating health impact in the risk areas more properly and exhaustively.

However, mortality represents the extreme event linked to several environmental and occupational exposures and the obtained results give a strong indication of the presence of adverse health effects that should not be neglected. In fact, it can be concluded, based on these results, that there are important health implications in the risk areas, more pronounced for men than for women. As indicated by the analysis of the seven areas combined, the excesses are bigger than can be expected by random fluctuations; causes of death are significantly in excess, and this applies to all causes, to large and small groups of diseases, and to most of the risk areas: around 300 excess deaths per year were observed in 1990–94.

Part of these excesses can be attributed to variations in lifestyle factors such cigarette smoking and diet. The influence of socioeconomic factors, although at least partially removed using the standardization by deprivation index, is likely to play a role. However, part of the excesses can be also associated with risk factors due to the presence of industrial facilities in the territory, as many studies have suggested. Most of the diseases, generally associated in the literature to occupational exposures, are in significant excess only for men (lung and bladder cancer, lympho-hematopoietic system) and most of the times they have been registered in risk areas characterized by the presence of chemical and petrochemical plants (Brindisi, Augusta-Priolo). More specifically, all the significant excesses of pleural cancer have been observed, both for men and for women, near locations characterized by important shipbuilding industries, and suggesting an occupational exposure to asbestos in dockyard workers, but also an environmental risk for the resident population.

These results, together with the growing concerns of the resident populations, suggest that continuous monitoring of the status of environment and health in risk areas is desirable. Further epidemiologic study of mortality in the risk areas is also important. This should be coordinated with local health authorities and researchers and integrated with more in-depth analyses, at smaller geographic aggregations as census tracts, especially where results indicate the presence of critical situations. More detailed data, besides mortality, are needed to identify proper corrective public health actions.

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