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Wasting lives: The effects of toxic waste exposure on health

The case of Campania, Southern Italy

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Abbreviations: Al, Aluminium; As, Arsenicum; Cd, Cadmium; CI, confidence interval; CB, cost benefit; Cu, Copper; DI, deprivation index; DNA, deoxyribonucleic acid; e.g., exempli gratia; ERR, excess relative risk; Fe, Iron; i.e., id est; ISTAT, Italian National Institute of Statistics; Km, kilometers; Mn, Manganese; PCDDs, polychlorinated dibenzop-dioxins; PCDFs, polychlorinated dibenzofurans; Pb, Lead; SWRI, synthetic waste risk index; TEM, transmission electron microscopy; V, Vanadium; VPF, value of prevented fatality; WHO, world health organization; WI, waste index; Zn, zinc

Three decades of illegal practices of waste dumping and consequent environmental abuse have made the Campania Region, Southern Italy, a unique case in the context of waste-related health outcomes. Scientific evidence is mounting in support of a significant increase in cancer mortality and malformation occurrence in specific areas of the Campania Region, where improper waste management and illegal waste trafficking have been repeatedly documented. However, the currently available evidence suffers from limitations mainly due to study design, lack of consideration of confounders and quality of the exposure data. Recent economic studies have shown the economic benefits of reclaiming toxic waste sites in Campania. Future perspectives include the adoption of different study designs, use of biomarkers and a molecular approach. Current knowledge, both scientific and economic, might be of help in orienting the short and long term governmental policy on waste related health outcomes at a regional level.

Introduction

Waste management encompasses a wide spectrum of functional elements including generation, processing, transport and disposal of solid waste material. The involved procedures might largely differ based on various determinants, such as waste characteristics (e.g. solid, liquid or gaseous substances), producer profile (residential vs. industrial producers) and involved area (high population density vs. low population density). Notwithstanding the general trend towards an increasing proportion of waste being recycled, disposal by landfilling still represents the most common ultimate fate of solid wastes.[1]

Residential proximity to waste disposals has been associated with adverse health outcomes. The available data mostly relates to cancer and birth outcomes, while data on respiratory, skin and gastrointestinal symptoms or diseases is still sparse.[2-6] Overall, the existing evidence does not rule out a clear role of landfilling in determining adverse health effects. In addition, the available data is substantially weakened by a number of methodological issues including inconsistencies in study design, use of surrogate measures of exposures (e.g. distance from the site of waste disposal), lack of control for potential confounders (i.e., factors correlated with both the exposure and outcome of interest, which do not lie on the causal pathway linking the exposure to the disease).[7]

Three decades of illegal practices of waste dumping and consequent environmental abuse have made the Campania Region, Southern Italy, a unique case in the context described so far. Since the 1980s, several illegal and uncontrolled sites of urban, toxic, and industrial waste disposal, including land filling and unauthorized incineration, have been known to be active in this Region, with the highest concentration being reached in the two provinces of Naples and Caserta. Results from a number of recently conducted studies have shown significantly increased cancer mortality (overall and site specific) and congenital malformation rates in the Provinces of Naples and Caserta compared to the expected figures from the regional population.[8-10] In the highlighted areas (i.e., the northern part of the Naples Province and the southern part of the Caserta Province), illegal dumping of toxic wastes has been largely documented.[11-12]

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In 1998, Agroaversano and Litorale Domizio, the two areas in Campania most affected by illegal dumping and burning, were included in the national priority list of reclamation sites. Since then, little has been done to clean up the contaminated areas.[13]

The task of quantifying the costs and the benefits arising from remedial interventions in monetary terms is pivotal to decisions regarding the prioritization of sites within the National Remediation Program.[14] Recent economic evaluations suggest that the high impact of hazardous waste exposure on human health in the two provinces of Naples and Caserta creates a strong economic incentive for reclaiming toxic waste sites (legal and illegal) in the Campania Region.[15]

In this review, we summarize and discuss the scientific evidence on waste exposure and health outcomes in the Campania region, with a specific focus on cancer mortality and congenital anomalies. We also discuss the results of the extensive biomonitoring activities conducted in Campania for a wide range of chemical agents (i.e., heavy metals, polychlorinated biphenyls, dioxins and polycyclic aromatic hydrocarbons). We then consider evidence from economic studies seeking to evaluate the economic benefit of reclaiming hazardous waste sites present in the Campania Region.

Evidence Linking Cancer Mortality and Congenital Anomalies to Waste Exposure in the Campania Region

In the early 2000s, the body of knowledge concerning the link between health outcomes and waste exposure in the Campania Region has grown notably. In 2001, Trinca et al. first drew the scientific community attention to childhood mortality in an area of the Caserta Province with several dumping grounds. In 2004, "The triangle of death", an area in Campania including the municipalities of Nola, Acerra and Marigliano, was described by Senior et al. Soon after, Bianchi et al. pointed out the complexity of the issue addressed and introduced the multidisciplinary group including WHO, the Italian Institute of Health in Rome, the National Research Council in Pisa, the Health and Environment Agencies of the Campania Region, which was entrusted by the National Department of the Civil Protection to conduct a large epidemiological investigation on health outcomes and waste cycle in Campania.[16-19]

The working group published its first results in 2006, within the frame of the study conducted by Comba and co-authors. The latter was a geographic study on cancer mortality and congenital anomalies assessed in 196 municipalities of the Provinces of Naples and Caserta. Standardized mortality ratios and Bayesian mortality ratios were computed and mapped for the outcomes of interest. According to the reported results, cancer risk and malformation occurrence were significantly increased in municipalities in the northern part of the Naples Province and in the southern part of the Caserta Province, compared with the expected figures from the regional population. Among the specific causes of cancer, excess risks were more frequently linked to liver, trachea, bronchus and lung, pleura and bladder. Urogenital and cardiovascular malformations were the most commonly represented among the congenital anomalies. In the identified area, there are numerous landfills and uncontrolled waste disposal sites.[11-12]

In 2008, Fazzo et al. published the results of a cluster analysis of mortality and malformations in the Provinces of Naples and Caserta. Analyses were standardized by Deprivation Index (DI), an indicator taking into account the possible role of socio-economic deprivation. More specifically, the DI is a national deprivation index suitable for geographical analysis of inequalities in health. Variables related to education, unemployment, housing ownership, surface of dwelling and family structure were used as selected indicators of inequalities. Such an index was built on figures from the 1991 Population Census and estimated at a municipal level.[20] Significant clustering of mortality by specific cancers (lung, liver, gastric, kidney and bladder) and prevalence of total and specific malformations (limb, cardiovascular, urogenital systems) were described in the northern part of Naples and southern part of Caserta Provinces, thus confirming the results by Comba et al.[8-9]

In the study by Martuzzi and co-authors, the intensity of waste-related exposure, as assessed throughout a composite index used at a municipality level, appeared to be correlated with several health outcomes. The waste index (WI) was built on data from the regional Environmental Protection Agency (including both authorized landfills and illegal waste dumping sites) and from the Italian National Institute of Statistics (ISTAT) 1991 Population Census. In brief, legal and illegal dumping sites were grouped into seven categories of decreasing hazard based on the likelihood of releases on water, soil and air. The use of a Geographic Information System allowed to divide the study area into circular zones traced around each site. Data on population counts by census tract were combined with the classification of the zones. A summary index was assigned to each municipality based on the sum of the zones included. Thus, by its nature, the WI accounted for the location and characteristics (in terms of potential hazard), impact area and population density in the surroundings of waste sites.

When comparing high-index with low-index municipalities, the authors observed statistically significant excess relative risks (ERR, %) for all-cause mortality (ERR% 9.2, 95% CI 6.5–11.9 and ERR% 12.4, 95% CI 9.5–5.4, in men and women, respectively). Increased risks were also found in both genders for all cancer mortality and liver cancer, while risks for stomach and lung cancer were significantly increased in men only. Statistically significant ERRs were also found for malformations of the urogenital system (ERR% 82.7, 95%CI 25.6–155.7) and of the central nervous system (ERR% 83.5, 95% CI 24.7–169.9). Risk estimates were adjusted for deprivation index, which was itself associated with several mortality outcomes in both genders.[21]

The use of a composite index as useful tool for the identification and characterization of areas where health risks from waste exposure are particularly high is the goal of a recent analysis conducted by Musmeci et al. Based on the assessment of a synthetic waste risk index (SWRI) computed at a municipality level throughout a multistep approach, the municipalities located along

Table 1. Epidemiologic studies on waste exposure and health outcomes (selected)

First Author, year, (reference)	Study design	Data sources	Outcome/s	Summary of findings
Comba et al., 2006[7]	Geographical study	ISTAT1, Regional Epidemiological Observatory of Campania, Campania Region Birth Defects Registry	All-cause mortality, Cancer mortality (overall and site specific), congenital anomalies	Significantly increased rates of all cause-mortality, cancer mortality and congenital malformations in the southeastern part of the province of Caserta and in the northwestern part of the province of Naples
Fazzo et al., 2008[8]	Geographical study	ISTAT, Campania Region Birth Defects Registry, 1991 Census	Cancer mortality, (overall and site specific), congenital anomalies	Significant clustering of mortality by specific cancers (lung, liver, gastric, kidney and bladder) and prevalence of total and specific malformations (limb, cardiovascular, urogenital systems) in the northern part of Naples and southern part of Caserta provinces
Martuzzi et al., 2009[9]	Geographical study	ISTAT, Campania Region Birth Defects Registry, 1991 Census, Environmental Protection Agency	All-cause mortality, cancer mortality, (overall and site specific), congenital anomalies	Significant excess relative risks (ERR, %) for all-cause mortality in men and women; increased risks in both genders for all cancer mortality and liver cancer; significantly increased risks for stomach and lung cancer in men only. Significant ERRs also found for malformations of the urogenital system and of the central nervous system
Musmeci et al., 2010[20]	Geographical study	2001 Census, Environmental Protection Agency	SWRI[2]	Municipalities along the border between the provinces of Caserta and Naples and located on the Tyrrhenian coast are exposed to higher waste-related health risk

[1]Istituto Nazionale di Statistica (Italian National Bureau of Statistics), [2]Synthetical Hazard Index.

the board between the Provinces of Naples and Caserta and on the Tyrrhenian side of the Campania coast appeared at higher waste-related health risk. The highlighted areas were previously identified by Comba et al. in referral to higher rates of cancer mortality and malformation occurrence, which were subsequently confirmed by Fazzo et al. Evidence on whether the SWRI correlates with mortality rates will be shortly available, thus adding significant insights to the possible use of this indicator in the evaluation of waste exposure on health outcomes.[9,22] **Table 1** summarizes the main characteristics and findings of the studies discussed so far.

Evidence Related to the Biomonitoring Activities Linked to Waste Disposal in the Campania Region

The ultimate objective of biomonitoring research is understanding the public health implications of exposure to environmental chemicals by linking biomarkers of exposure to biomarkers of effect and susceptibility.[23] Biomonitoring research includes a wide range of approaches, potentially ranging from the use of sentinel organisms, as prospectors and integrators of information on environmental risk assessment, to the measurements of biomarkers of exposure in humans.

Biomonitoring holds great potentials in regards to the assessment of waste exposure-related outcomes. Unfortunately, in strict referral to the Campania Region, the inherent scientific panorama is particularly restricted. In May 2011, we electronically searched MEDLINE (1966-onwards) by combining terms related to biomonitoring, pollution and Campania Region. Our search yielded two results only. Additional evidence suitable to the purposes of this review was provided by the 2010 report from the SEBIOREC study.[24-26]

Bioaccumulation studies are based on the well documented capacity of some organisms, mainly lichens and mosses, to modify their parameters when exposed to pollutants. Independently on the specific mechanisms regulating the uptake and accumulation of the single elements, these bioaccumulators may quite reliably reflect the characteristics of the surrounding environment.[27]

Basile et al. used mosses for determining heavy metal air pollution in the area of Acerra. Mosses can be used as bioaccumulators of airborne heavy metals due to the lack of a root system. The latter explains the strict dependence of mosses on atmospheric depositions for mineral supply, particularly heavy metals. Samples of *Scorpiyurum circinatum* were exposed for 1–3 months in 20 sites of Acerra grouped by site type (urban, industrial and agricultural), while reference samples were stored in the Herbarium of the Botanical Garden of the Federico II University of Naples. Mass spectrometry was used to evaluate bioaccumuling of heavy metals (Al, As, Cd, Cu, Cr, Fe, Pb, Mn, V, Zn) and ultrastructural observation was performed throughout transmission electron microscopy (TEM).

For all the heavy metals and at all the three site types, the authors observed significantly higher element concentrations in exposed samples compared to controls after only one month of exposure ($p < 0.05$). The increase in heavy metal content was constant and linear throughout the whole exposure period. The ultrastructural analysis by TEM revealed an overall preserved

organization. However, the authors described the presence of membrane pits, cytoplasm vesicles and concentric multilamellar/multivesicular bodies, which were ascribed to tolerance mechanisms to metal pollution.[24]

Genetic ecotoxicology is the study of pollutant-induced genetic changes in exposed organisms.[28] DNA damage may result from the exposure to xenobiotics, including air pollutants. Amphibians exhibit a variety of adverse effects from environmental exposure and can be used as sentinel species when investigating environmental risks at contaminated sites.[29-31] Maselli et al. used frogs to evaluate DNA damage related to pollution in Naples and neighboring Provinces. Twenty frogs were sampled from several sites of the Campania Region, including areas in the close proximity of dumping sites (both legal and illegal), sites influenced by intensive farming and uncontaminated sites. An adjunctive sample of 20 frogs collected from the Lao river was included as external control. The alkaline single cell gel electrophoresis assay, or comet assay, was used to measure and analyze DNA breakage in individual cells. The frogs sampled from the northern area of Campania showed particularly severe DNA damage, with the highest genotoxicity being shown in animals collected in proximity of waste dumping sites.[25,32]

SEBIOREC is an epidemiologic study of biomonitoring conducted in Campania between 2007 and 2010. The study aimed to assess the exposure to several organic and inorganic contaminants in biological samples from healthy donors. Blood and milk samples were collected, handled and analyzed according to highly standardized procedures. Ad hoc questionnaires focusing on medical history, lifestyle, occupational and (in women) reproductive history were administered. Individual blood sample from 423 male and 436 female donors, serum samples from 429 male and 447 female donors and 62 milk samples from primipaurous women were combined into 84 blood pools, 84 serum pools and 7 milk pools.

Based on previous work, municipalities were grouped by index of waste environmental pressure into three main areas or zones. Zone A, B and C were defined at intense, medium and low environmental pressure, respectively.[10,22,33] When performing analyses, data subsets were compared by numerous variables, including areas differing by degree of environmental pressure due to waste (i.e. zones A, B and C). The latter variable seemed to significantly affect the circulating levels of a limited number of contaminants, i.e. serum concentrations of PCDDs and PCDFs, among the organic contaminants, and blood levels of Cd, among the heavy metals. More specifically, data showed significant differences in PCDDs and PCDFs between zones A and C and zones B and C. In referral to Cd, there was a marginally significant difference between zones A and B.[26]

Evidence From Economic Studies Evaluating the Economic Benefit of Reclaiming Hazardous Waste Sites in Campania

Cost Benefit (CB) analysis is a transparent tool for evaluating the social worth of remedial interventions. If the cleanup cost is outweighed by the estimated benefit, i.e., the net benefit is positive, the intervention is deemed worthwhile. CB analysis is also performed to identify the most appropriate cleanup technologies (e.g. capping versus on site excavation) or to prioritize contaminated sites for reclamation.

Using epidemiological data from the correlation study conducted by Martuzzi et al., Guerriero and Cairns monetized the potential health benefits of reclaiming hazardous waste sites in the two provinces of Caserta and Naples. The study found that every year there are 848 cases of premature death. Among these, 403 were cancer related deaths. The study assigned a value of a prevented fatality (VPF) to each health case attributable to waste exposure according to values suggested by the European commission for conducting environmental cost benefit analysis. Assuming that mortality reductions would be displayed 20 years after remediation, and that they will last for 30 years, Guerriero and Cairns estimated that reclaiming the hazardous waste sites present in the two provinces of Naples and Caserta would produce a monetary benefits of €11.6 billion (range: €5.4-20 billion).[10,15]

In 2010, Alberini et al. revisited the Guerriero and Cairns study applying both VPF values and discount rate estimated in Italy to the specific context of hazardous waste exposure. Using parameters specific to the Italian context, the study concluded that the potential monetary benefits achievable through waste sites cleanup was even greater than that reported by Guerriero and Cairns: €12.936 billion.[34]

In both studies, the benefit estimates were considerably higher than the cost, €143 million, agreed by the Government for the remediation of the hazardous waste sites in the two provinces of Caserta and Naples.

Discussion

As presented in this review, there is consistent epidemiologic evidence in support of the association between health outcomes and waste exposure in the Campania Region. Cancer mortality (overall and site specific) and congenital malformation rates appear to be significantly increased in the northern part of the Naples Province and in the southern part of the Caserta Province, compared to the expected regional figures. In these areas, the presence of numerous dumping sites (both legal and illegal) has been repeatedly documented.[8-12,22] Though suggestive of a contributory role of waste exposure in determining health outcomes in the identified areas, these findings are far from being conclusive relatively to the causative nature of the association observed. In the first place, the adopted study designs do not allow causal inference. Indeed, as pointed out by the authors themselves, the geographical and correlation studies conducted so far were not conceived for the assessment of causal-effect relationships. They rather represent the first step towards the construction of a more complex epidemiologic framework which will be integrated by clinical and toxicological expertise to ultimately clarify causal issues. The second issue involves confounding. Lack of adjustment for confounders is quite common in studies related to waste exposure, particularly those relying on a geographical design. In the attempt to overcome such a limitation, the Deprivation Index, an indicator of socio-economic status, was included in the

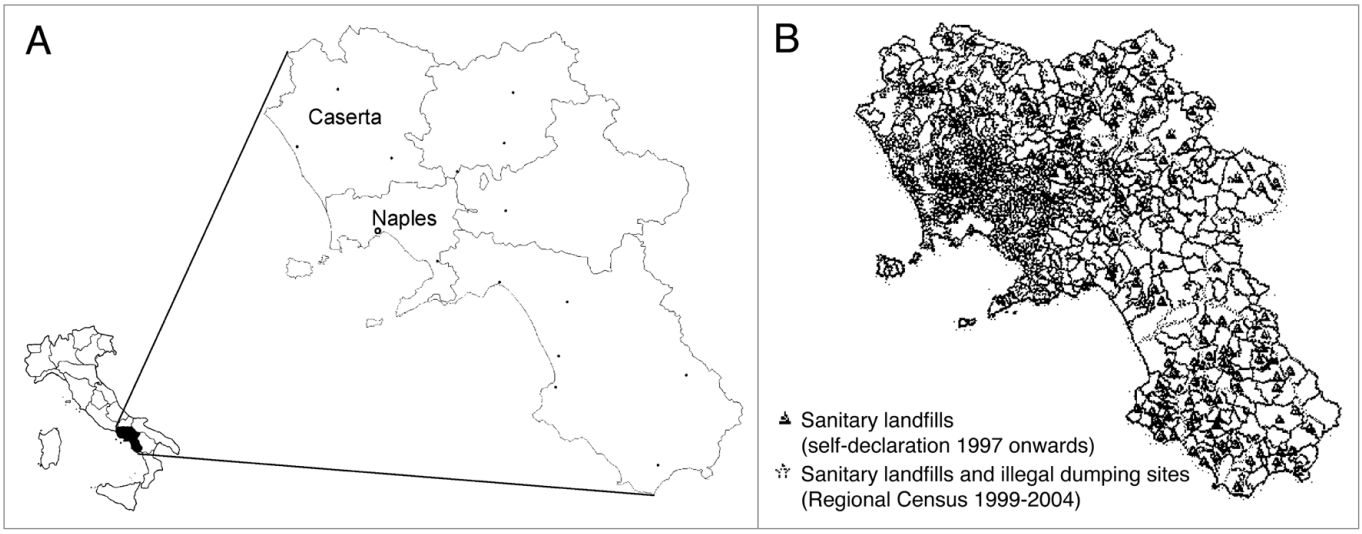

Figure 1. Geographical distribution of waste sites in Campania, Southern Italy. The rightmost panel is from Fazzo et al., 2008.[9]

analyses conducted in at least two of the studies mentioned.[9-10] This approach finds support in the large and consistent evidence indicating a tendency of socio-economically disadvantaged populations and minority groups to be overrepresented in areas surrounding waste disposal sites.[35] However, in the studies conducted by Fazzo and Martuzzi, residual confounding from risk factors other than socioeconomic determinants cannot be excluded.

The third issue relates to data quality in referral to both the disease outcomes and exposure of interest. In regards to the disease outcomes, data quality and completeness represent key issues which affect reliability and potential data use. In such a context, Martuzzi et al. invite to caution when interpreting evidence linking waste exposure to congenital anomalies. This is due to the quite large but still not complete percentage of coverage of all deliveries from the Campania Region registry of congenital anomalies, which was used as data source for malformations.[10] Similar considerations stem from the use of data from cancer registries for cancer related outcomes (e.g., cancer mortality and incidence). Indeed, cancer registries cover a quite restricted proportion of the Italian population (i.e., about 34%), with a notable imbalance between Northern, Central and Southern areas.[36] In a recently published paper, Piscitelli et al. underline the need to integrate data from cancer registries with additional sources and identify the National hospital discharge records database as an appropriate tool to help overcome the limitations of the Italian network of local cancer registries.[37]

When addressing waste exposure in the Campania region scenario, the question of data quality and completeness becomes paramount. In recent years, the body of knowledge concerning the geographical distribution of waste sites has grown rapidly (**Fig. 1**). Still, most of the disposals are not visible (sunken or buried) and there is limited (not to say null) information on the nature of the toxic substances contained.

Evidence from biomonitoring is still sparse and not always consistent. While data from studies conducted in sentinel organisms seem to be indicative of different types of particularly severe damage in samples collected in proximity of waste dumping sites, the results of a large biomonitoring study conducted in Campania, the SEBIOREC study, are only partially supportive. Indeed, the analysis of data subsets by degree of environmental pressure due to waste showed a significant impact of the latter variable on the serum/blood levels of a quite restricted number of contaminants (i.e. PCDDs and PCDFs, among the organic contaminants, and Cd among the heavy metals). This might be at least partly explained by the quality of the exposure data, as discussed above. On this basis, exposure misclassification may be hypothesized.[24-26]

Studies based on individuals rather than communities represent the way forward for future evaluations of potential health effects related to waste management in Campania. The use of biomarkers as useful tools in exposure assessment is desirable, even though the high number and heterogeneous nature of contaminants add substantial complexity to this task. Biomarkers might help reduce misclassification and contribute to identify lower level exposures and the total burden of exposure. The identification of health events earlier in the natural history of the diseases and insight into the mechanisms relating exposure and disease might be adjunctive advantages deriving from the use of biomarkers. Further insight in the disease etiopathogenesis, for diseases related to waste exposure, might derive from the field of molecular epidemiology. The latter offers the opportunity to combine epidemiology with molecular toxicology to investigate interactions between genetic determinants and environmental factors and identify high risk groups.

Summary and Conclusions

In summary, scientific evidence is mounting in support of the association between waste exposure and health outcomes in specific areas of the Campania Region, where improper waste management and illegal waste trafficking have been repeatedly

documented. However, the currently available evidence suffers from limitations mainly due to study design, lack of consideration of confounders and quality of exposure data. The adoption of different study designs, use of biomarkers and a molecular approach might greatly improve the quality of the upcoming studies. In recent years, the use of a multidisciplinary approach integrating epidemiologic and economic expertises has produced impressive results. The net monetary benefits deriving from the reclamation of hazardous sites present in Campania would be considerably higher than the estimated costs. In a recent study of the effects of US superfund cleanups on human health, the authors observed a 20–25% reduction of congenital anomalies in residents of areas where the remediation of contaminated sites took place. Such a decrease has an equivalent in terms of lives saved and quality of life for future generations. The same goals need to be pursued in the Campania Region.[38]

In conclusion, the scientific panorama, along with the results of economic studies, encourage further investigation on the topic addressed. Considering the results of such studies is a must in orienting the short and long term governmental policy on waste related health outcomes at a regional level.

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