

*Review Article*

Hazardous wastes in Campania (Italy) and health impact

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During the 1980s, the region of Campania (particularly Naples and Caserta) underwent illegal dumping of toxic waste. In this regard, adverse health outcomes of this population could increase and contribute to risk of diseases. The highly toxic waste (HTW) dumping along the coast and the hinterland has led to high rates of congenital disabilities and cancers. In this context, the waste derived from hospitals, mining, agriculture, petroleum refining, textile, chemical, construction, and food processing industries has contaminated the land. It has caused the local population to have high exposure to toxic waste. In addition, the scientific community tried to show a relationship between exposure to pollutants and health issues. Here, we point out the importance of epidemiological and biomonitoring data from an environmental perspective to address the correlation between long-term exposure to different pollutants and consequences on human health.

Keywords: Toxic waste, Human Health, Cancer, Campania, Naples and Caserta**INTRODUCTION**

Disposal and management of waste is becoming a significant issue around the globe. Specifically, illegal dumping of urban and hazardous waste disposal is practiced by local communities in all countries by including illegal transboundary trade, mostly from industrialized countries.^[1] In this regard, many studies underlined the potential correlation between unsafe and illegal waste management and the increase of diseases of waste-related exposures in several countries. Waste management is a challenging task in all European countries, with an important impact on human health and well-being, environmental preservation, and sustainability. In many cases, uncontrolled or unsafe waste practices can produce adverse human health effects, such as a documented increase of cancer risk. An overall estimate of these impacts is not available, and exploratory work suggests that annoyance may outweigh the other effects in terms of the burden of disease. In 2016, hazardous waste accounted for about one-quarter of Europe's approximately 350,000 contaminated sites. In this regard, the lack of systematic data from non-EU countries makes it difficult to develop a pan-European assessment and direct the necessary efforts, expertise, and resources towards countries that could improve.^[2] In April 2021, the US Environmental Protection Agency's National Priority List (NPL) identified more than 1,300 Superfund sites (New

Jersey 114 followed by California and Pennsylvania, which had 97 and 90 sites, respectively).^[3] In developing countries, many studies pointed out that hazardous waste was burned in the open air^[4-6] and illegally recycled, threatening human health and the environment. For example, in seven Asian countries, 769 areas are at high risk for contaminated sites. Furthermore, approximately 250,000 children (0.4 years old) live close to the contaminated sites (169) containing lead (Pb) at high levels. Pb poisoning—a consequence of exposure to Pb—can provoke disease of the central nervous system and developmental delays.^[7] In this regard, children and pregnant women are vulnerable to health effects.^[8] Two studies calculated the burden of disease resulting from Pb exposure using the disability-adjusted life year (DALY). Such tests considered the disease burden of illness, injury, and death due to environmental toxicant exposure.^[9,10] In the first study, Chatman-Stephens and colleagues reported that 0.22% of the total estimated DALYs were attributed to pollutants found at hazardous waste sites in India, Indonesia, and the Philippines.^[9] The second study carried out in Argentina, Mexico and Uruguay, showed that 316,703 persons were exposed to pollutants. Particularly, the authors observed that exposure to lead resulted in between 51,432 and 115,042 DALYs, depending on the weighting factor used.^[10] In Africa, the World Health Organization (WHO) calculated

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that one-third of the increased disease could be correlated to environmental risk factors.^[11,12] For example, in most African cities, 20% of urban waste is disposed of in landfills and 80% in illegal dumps.^[13] Furthermore, yearly, the waste electrical and electronic equipment production (widely known as WEEE or e-waste) is increasing rapidly. Hazardous constituents of such waste can negatively influence both environment and human health, if not properly managed. In this regard, developed countries generate much e-waste that is illegally exported to developing countries, where they are recycled in an unsafe manner.^[14,15] Several investigations underlined the negative impact on health in local populations living near hazardous waste dumping sites in recent years. In 2000, a review of Vrijheid showed the results of 50 papers published from 1980 through 1998.^[16] These epidemiological studies examined chemicals released into the environment by waste disposal sites.^[16] Ecological and geographical studies showed an increased risk of different types of cancer, mainly both men and women- lung cancer in men and women,^[17-20] bladder cancer in both sexes,^[21,22] leukemia was primarily found in men,^[23] childhood leukemia was also prevalent,^[24] liver cancer in men,^[18] prostate cancer,^[18] gastric cancer in both sexes,^[17] uterine cancer,^[18] rectum cancer,^[3] and breast cancer.^[17] Although many studies have been conducted, but the evidence of a causal relationship between hazardous waste and cancers “is still weak,” with regards to specific cancers reported in more than one study, mainly leukemia, bladder, lung, and stomach.^[16] Another review on epidemiological studies conducted on population living close to hazardous waste sites showed an increase in the frequency of diverse types of cancer. The author concluded that it was challenging to determine the association between the residence near hazardous waste sites, and increased cancer incidences.^[25] For more than a decade, toxic wastes in the region of Campania were disposed of illegally. Different studies are carried out on the local population to better underline the high rate of mortality and morbidity observed in the region. This review analyzes the results from published articles^[3] on cancer, childhood mortality, and human biomonitoring to identify and prioritize research gaps.

MATERIAL AND METHODS

We considered scientific literature articles, news from journals, and media reports. The data collection was based on different categories: (a) illegal dumping of toxic waste in Campania, specifically in Naples and Caserta provinces; (b) cancer rate; (c) epidemiological studies in Campania, specifically in Naples and Caserta province; (c) exposure and biomonitoring studies in the population living in Campania (d) the land of fire and (e) the triangle of death. Different databases are used, including Scopus (scopus.com), Web of

Science (webofscience.com), Google Scholar, and PubMed Central (PMC). We obtained many papers using keywords such as “Illegal waste,” cancer mortality and Campania and Naples and Caserta provinces Environmental exposure, Biomonitoring Epidemiological risk, and illegal waste dumping. Then, we selected articles in the English language and analyzed them, considering the chosen keywords.

RESULTS

Multiple studies in Campania tried to analyze a relationship between exposure to toxic waste and morbidity patterns. However, it was challenging to demonstrate this association since many cancer types have multifactorial pathogenesis. Furthermore, many toxic pollutants are unknown due to improper and illegal disposal. We examined articles that evaluated different kinds of cancer, such as liver, lung, larynx, bladder, leukemia, colorectal cancer, sarcoma and Central Nervous System (CNS), gastric, and kidney. We found nine papers on human biomonitoring: five on exposure biomarkers and four on early effect biomarkers. Some studies were conducted on people living close to illegal landfills with high levels of dioxins and polychlorinated biphenyls (PCB) in blood or human milk samples. Other papers reported a reduction of sperm motility and decreased telomere length in the semen of men living in contaminated areas. One summary table showed the article on cancer rate mortality [Table 1].

Toxic waste pollution in Campania and cancer incidence

Some reports published by international agencies such as the United Nations Environmental Program (UNEP) and Greenpeace showed that much highly toxic waste derived from Italian and foreign companies was disposed of in Campania illegally. In 2004, K. Senior and A. Mazza²⁶ published some results on the association between environmental pollution and cancer-related deaths in the Nola area in the prestigious journal “The Lancet Oncology.” The districts of Senior and Mazza reported high mortality rates for colorectal and liver cancer, leukemia, and lymphoma, as compared to the rest of Campania and Italy. Furthermore, Mazza reported the high environmental risk among the Neapolitan towns of Acerra, Nola, and Marigliano^[26] [Table 1]. In this scenario, several studies were performed in order to find the link between toxic waste and the high incidence of different types of cancer. One study was carried out between 1998 and 2001 in the five provinces of the Campania region (Salerno, Avellino, Benevento, Naples, and Caserta) that estimated the standardized mortality ratio (SMR). Pizzuti and colleagues observed that the age-adjusted SMRs for all cancers were higher in the Naples and Caserta provinces when compared with other provinces (Salerno, Avellino, and

Table 1: Studies on human health impact in Campania region to date.

Authors	Study Subjects	Health Outcomes	Reported Data
Senior and Mazza (2004) ^[26]	250,000 people living Acerra, Nola, and Marigliano	Cancer Mortality rate	All cancers ¹ SDR = 321.7 (Male-District 73) vs. Regional rate 305.6 (Male) Liver SDR = 35.9 (M D-73) vs. regional rate 15.0 Larynx SDR = 12.8 (M district 73) vs. Regional rate 8.7 (Male) Bladder SDR = 29.3 (M District 73) vs. regional rate 21.7 (Male) Colorectal SDR = 29 (Female District 73) vs. Regional rate 26.4 (Female) Leukemia and lymphoma SDR = 28.2 (Male District 73) (vs. SDR = 17.9 (Male ASL 4) (Male); SDR = 18.7 (Female 18.7 District 73) vs. rate 16.1 (Female ASL 4)
Pizzuti et al. (2005) ^[27]	Inhabitants of Campania (1998 to 2001)	Increased cancer Mortality(1988 to 2001) in Caserta and Naples compared with other cities of Campania	² SMRs All Cancers Caserta 104.9/106.1 (M/F) Naples 109.3/108.3 (M/F) Avellino 83.6/84.9 (M/F) Benevento 84.8/82.4 (M/F) Salerno 91.0/90.8 (M/F) Liver Caserta 97.7/100.8 (M/F) Naples 123.9/120.8 (M/F) Avellino 60.3/59.1 Benevento 53.8/97.7 (M/F) Salerno 79.5/85.7 (M/F) Stomach Caserta 135.5/122.9 (M/F) Naples 102.6/101.0 (M/F) Avellino 102.4/86.9 (M/F) Benevento 86.9/107.4 (M/F) Salerno 75.0/84,6 (M/F)
Altavista et al. (2004) ^[28]	150,000 Inhabitants living in municipalities of Naples (Giugliano, Qualiano, and Villaricca) (1986–2000)	Cancer Mortality rate	Giugliano All cancers SMR 107,23 (M) SMR = 111,08 (F) Liver SMR 181,13 (F) Lung SMR 121,85 (M) and SMR 112,23 (F) Pleural SMR = 267,77 (M) SMR = 370,05 (F) Bladder SMR = 130,12 (M) Larynx SMR = 339,42 (F) Qualiano All cancer SMR = 111,78 (M) SMR = 99,66 (F) Larynx SMR = 211,85 (M) 261,39 (F) Villaricca All cancer SMR = 106,73 (M) 109,85 (F) Liver SMR = 36,80 (F) Stomach SMR = 56,06 (M) Lung SME = 120,94 (M) SMR = 176,84 (F) Pleural SMR = 432,68 (M) SMR = 266,68 (F) Brain SMR = 195,41 (F);

(Continued)

Table 1: (Continued)

Authors	Study Subjects	Health Outcomes	Reported Data
Comba <i>et al.</i> , (2006) ^[29]	4 million people in 196 municipalities of Caserta and Naples (1994–2001)	Cancer Mortality Rate	Naples Provinces All cancers SMR = 108.7(M) SMR = 109.2 (F) Liver cancer SMR = 117.6 (M) SMR = 114.1 (F) Larynx Cancer SMR = 111.8 (M) Trachea, bronchus, and lung Cancer SMR = 114.1 (M) 1,845 SMR = 126.5 (F) Pleura Cancer SMR = 132.9 (M) SMR = 125.8 (F) Bladder Cancer SMR = 110.7 (M) SMR = 117.5 (F) Caserta Province All cancers SMR = 102.3 (M) SMR = 98.2 (F) Stomach cancer SMR = 129.3 (M) SMR = 118.2 (F)
Martuzzi <i>et al.</i> , (2009) ^[30]	4 million people in 196 municipalities of Caserta and Naples (1994–2001)	Cancer Mortality Rate	all cancers (M) 4.2 (1.1 to 7.5) (II 95% CI); 5.6 (0.8 to 10.6) (III 95%) 4.9 (1.3 to 8.5) (IV 95%) 4.1 (20.5 to 8.9) (V 95%) 1.5 (0.6 to 2.3) Trend 95% CI 4.4 (3.6 to 5.2) Trend 95 % CI for DI All cancers (F) 5.1 (1.3 to 9.1) (II 95% CI) 2.4 (23.3 to 8.5) (III 95% CI) 3.6 (20.8 to 8.1) (IV 95% CI) 6.6 (0.8 to 12.7) (V 95% CI) 1.0 (0 to 2.1) (Trend 95% CI) 3.4 (2.4 to 4.4) (Trend 95 % CI for DI) Liver Cancer (M) 19.3 (1.4 to 40.3) (V 95% CI) 4.9 (3.4 to 6.4) (Trend 95% CI DI) Liver Cancer (F) 29.1 (7.6 to 54.8) (V95% CI) 4.7 (1.1 to 8.5) (Trend 95% CI DI) Stomach cancer (M) 19.4 (4.5 to 36.4) (IV 95% CI)
Fazzo <i>et al.</i> , (2008) ^[31]	4 million people in 196 municipalities of Caserta and Naples (1994–2001)	Cancer Mortality Rate	Lung Cancer Calvizzano (9 municipalities) 1008 cases Casalnuovo di napoli (8 Municipalities) 1002 cases Liver cancer Acerra (18 mun) 506 cases (417 in male population). Capodrise (2 mun) 91 cases Roccarainola (5 mun) 58 cases (35 cases in male population) Marcianise (1 mun) 53 case (M) San Cipriano di Aversa (1 mun) 18 cases (M) Marigliano (1 mun) 35 in female population Gricignano di Aversa (36 mun) 351 cases in female population Stomach Cancer Teverola (1 mun) 615 cases (383 in male population) Bladder Cancer Marano di Napoli (11 mun) 206 cases (174 in male population). Casagiove (11 mun) 161 cases

Authors	Study Subjects	Health Outcomes	Reported Data
Fazzo <i>et al.</i> (2011) ^[32]	5 million people living in 35 municipalities of Naples Province (1997–2005)	Cancer Mortality Rate	The authors found increased cancers (liver and lung cancer, non-Hodgkin's lymphoma (NHL), and total leukemia) in both genders. In the male population, the authors found an increased incidence of the testis, esophagus, larynx, pancreas, thyroid gland cancer, and morphologic soft-tissue sarcomas, while in the female population, for stomach and topographic soft tissue sarcomas. Kidney, biliary ducts, brain cancer, and myeloma increased in all populations.
Pirastu <i>et al.</i> (2011) ^[33]	1314222 Inhabitants 77 municipality of Caserta and Naples provinces (Litorale Domizio Flegreo e Agro Aversano) and 462322 Inhabitants of 11 municipalities of Naples provinces (Area Litorale vesuviano) (SIN - Sito di Interesse Nazionale ai fini di bonifica 2001)	Cancer Mortality	Number of observed cases (OSS) of cancers (OSS) were 11 292 (Male); The Cancer Number of observed cases (OSS) of cancers was 7 116 (Female) regional reference (1995–2002)
Comba <i>et al.</i> (2014) ^[34]	People living in 55 municipalities of the "Land of Fires" (2007–2010)	Cancer incidence and mortality	Increase of hospitalization and mortality rates for different types of cancer in Caserta province (stomach, liver, lung, bladder, laryngeal cancer, and leukemia) and Naples province (stomach, liver, lung, bladder, pancreatic, laryngeal, kidney, breast cancer, and non-Hodgkin's lymphoma)
Di Lorenzo <i>et al.</i> , (2015) ^[35]	People living In the province of Naples and Caserta	Cancer Incidence and Mortality	The mortality and incidence of bladder cancer were high when compared with regional data in the province of Naples and some regions of the province of Caserta,
Zona <i>et al.</i> (2019) ^[36]	1314222 Inhabitants 77 municipalities of Caserta and Naples provinces (Litorale Domizio Flegreo Agro Aversano SIN - Sito di Interesse Nazionale ai fini di bonifica 2001) 462.322 Inhabitants in 11 municipalities of Naples province (Litorale Vesuviano SIN 2001)	Cancer Incidence and mortality	Cancer Mortality (2006–2013) in LDF Liver Cancer SMR = 115 (90% CI (110–120) (M) SMR = 114 (90% CI (107–121) (F) Breast Cancer SMR = 105 (90% CI (101–1099) (F) Bladder Cancer SMR = 111 (90% CI (105–117) (M) Stomach Cancer SMR = 122 (90% CI (115–129) (M) SMR = 119 90% CI (111–127) (F) Colorectal Cancer SMR = 105 (90% CI (100–110) (M) SMR = 107(90% CI (102–113) (F) Cancer Mortality (2006–2013) in ALV Cancer Mortality/2006–2013) Liver Cancer SMR = 129 (90% CI 120–138) (M) SMR = 137 (90% CI (125–150) (F) Breast Cancer SMR = 110 (90% CI (103–117) (F) Bladder Cancer SMR = 111 (90% CI (105–117) (M) SMR = 104 (90% CI (91–118) (F) Cervix Cancer SMR = 116 (90% CI (102–131) (F)

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Table 1: (Continued)

Authors	Study Subjects	Health Outcomes	Reported Data
Indinolfi <i>et al.</i> (2016) ^[37]	1,014,796 children between 0–15 years old. in Campania Region for 25 years	Cancer incidence	During the 1990 and 2014 years, the authors found 3655 cancer cases were reported (Napoli province 2059 cases, Salerno province 625, Caserta province 589, Avellino province 229, and Benevento province 153).
Piscitelli <i>et al.</i> (2017) ^[38]	2362 hospitalizations in pediatric patients (0–19 years old) of all tumors. (2007–2011)	Cancer Incidence	The study found 3.465 cases of cancers in Campania in pediatric age (0–19 years) between 2007–2011.
Zona <i>et al.</i> (2023) ^[40]	1432475 Inhabitants 77 municipalities of Caserta and Naples provinces (Litorale Domizio Flegreo Agro Aversano SIN- Sito di Interesse Nazionale ai fini di bonifica 2001) 426777 Inhabitants in 11 municipalities of Naples province (Litorale Vesuviano SIN 2001)	Cancer Incidence and mortality	<p>Mortality Cancer (2014–2018) in LDF</p> <p>Liver Cancer SMR = 114(108–121) (M) SMR = 131 (121–142) (F)</p> <p>Breast Cancer SMR = 166 (113–224) (M) SMR = 106 (100–11) (F)</p> <p>Testis Cancer SMR = 36(19–70) (M)</p> <p>Bladder Cancer SMR = 96 (86–107) (M) SMR = 108 (95–125) (F)</p> <p>Non-Hodgkin Lymphoma SMR = 96 (86–107) (M) SMR (107 (94–121) (F)</p> <p>Mortality Cancer (2014–2018) in ALV</p> <p>Liver Cancer SMR = 117 (107–129) (M) SMR = 154 (137–173) (F)</p> <p>Lung Cancer SMR = 109 (104–115) (M) SMR = 105 (95–1159) (F)</p> <p>Mesothelioma SMR = 240 (190–302) (M) SMR = 87 (47–161) (F)</p> <p>Mesothelioma of pleura SMR = 243 (186–317) (M) SMR = 69 (31–153) (F)</p> <p>Breast Cancer SMR = 111 (102–120) (F)</p> <p>Cervix and uterus cancer SMR = 122 (104–142) (F)</p> <p>Testis Cancer SMR102 (50–209) (M)</p> <p>Bladder cancer SMR = 110 (98–123) (M) SMR = 115 (92–144) (F)</p> <p>Non-Hodgkin Lymphoma SMR = 115 (96–137) (M) SMR = 101 (95–108) (F)</p>

Standardized death rates (SDR) per 100000 population; Age-adjusted standardized mortality ratios (SMRs); standardized incidence ratios (SIR); ASL: Local Sanitary District of Naples 4; CI: Confidence Interval; DI: Deprivation Index; Mun: Municipality; OSS: Number of Observed Cases; ALV: Area Litorale Vesuviano; MD/M: District: Male-District

Benevento). Specifically, the authors detected the highest SMR values for stomach and liver cancer in Caserta and Naples provinces^[27] [Table 1]. Altavista *et al.*^[28] showed that the mortality rate among citizens living in the Giugliano, Villaricca, and Qualiano municipalities (51 km²) were higher when compared with those expected based on the regional data provided by Istituto Nazionale di Statistica (ISTAT). Specifically, the authors found a cancer high standardized mortality ratios (SMRs) in the population of Giugliano. In addition, increased standardized mortality ratios were observed for different types of cancer, such as lung, brain, liver, larynx, and pleural cancer, in the populations of Qualiano and Villaricca^[28] [Table 1]. Another study analyzed the cancer mortality in a population of approximately 4 million citizens living in 196 municipalities in Naples and Caserta. In this paper, the authors reported an increased mortality rate of pleural cancer in the male population and of esophageal cancer in the female population in the province of Naples. Moreover, in the province of Caserta, the authors showed an increased mortality rate for different types of cancer, such as the stomach (29.3% in the male population and 18.2% in the female population). In addition, the authors pointed out that the cancer death rate increased in 11 municipalities of the southeastern part of the Province of Caserta and 13 adjacent municipalities of the northern part of the Province of Naples^[29] [Table 1]. Moreover, another research was conducted in the same municipalities by estimating the environmental contamination through waste exposure at a municipal level using the regional database of legal waste landfills, and illegal dumping sites after adjustment for social and economic factors. In particular, this study used the Environmental Waste Index (EWI), which considered population density, distance to a waste site, volume and type of waste, and routes of contamination (e.g., food, air, or water). Furthermore, the authors performed the adjustment by the socioeconomic factors (such as education, income, and employment) through an index of socioeconomic deprivation (ID-municipalities that were subdivided into quintiles concerning the value of the deprivation index (1 = least deprived; 5 = most deprived) into a regression model. The authors observed a higher risk of cancer mortality in municipalities with high EWI than those with low EWI for all cancers (both sexes). They specially found mortality risk in the male population caused due to liver, stomach, and lung cancer, whereas in the female population, the risk was primarily due to lung and liver cancer^[30] [Table 1]. Another study was conducted 31 [Table 1] in the same municipalities (classified following a scale of 1 to 5, considering different factors such as high environmental pressure and increased mortality for cancer), Fazzo *et al.* found a statistically significant risk of cancer mortality rate in the provinces of Naples and Caserta^[31] [Table 1].

The authors found two clusters of lung cancer in the municipalities of Caivano e Casalnuovo di Napoli. Furthermore, the authors reported two clusters in the male population considering the municipalities of Calvizzano and Sant'Anastasia (8 municipalities), with 876 and 496 cases, respectively. Three clusters of liver cancer were detected in the Acerra, Capodrise, and Roccarainola municipalities. In the case of the male population, 4 clusters were identified in the municipalities of Acerra, Marigliano San Cipriano D'aversa, and Roccarainola. Meanwhile, only 2 clusters were described in the female population, specifically in the Marigliano and Gricignano di Aversa municipalities. Moreover, a large cluster of stomach cancer was detected in Teverola. Finally, two clusters of bladder cancer were reported in Marano di Napoli and Casagione^[31] [Table 1]. Furthermore, Fazzo *et al.* in 2011^[32] calculated municipal standardized incidence ratios (SIR) and hierarchical Bayesian estimators (BIR) in 35 municipalities of Campania through the Cancer Registry. Moreover, they considered municipal spatial clustering and a Poisson regression by municipality index of waste-related exposure for 10 kinds of cancer. In addition, they performed an Environmental Waste Index (EWI), considering socioeconomic factors through an index of socioeconomic deprivation (ID-municipalities). In this study, they found a statistically significant cluster for different cancers (liver, lung, leukemia, soft tissue sarcomas, and, in addition, testis)^[32] [Table 1].

In line with these studies, SENTIERI Project^[33] [Table 1] (studies mortality of residents living close to sites of national interest for environmental remediation - Italian polluted sites, IPSs that are located in the vicinity of industrial areas, either active or dismissed, near incinerators or dumping sites of industrial or hazardous waste) found high-risk mortality for liver larynx cancer in males; in the 77 municipalities of Caserta (Litorale Domizio Flegreo) and Naples Provinces (Agro Aversano).^[33] In addition, in the Litoral Vesuviano area, this report found an excess of liver cancer tumors for both sexes, as reported in other studies.^[19,20,31] Furthermore, the authors described an increased risk of pleural and lung cancer in this area correlated with the presence of asbestosis (as indicated in IPSs)^[33] [Table 1]. This research underlined an increased mortality risk for all cancers in the 77 municipalities of Caserta and Naples Provinces (Litorale Domizio Flegreo e Agro Aversano) in comparison with mortality expected from the Italian rate in females^[33] [Table 1]. Within the SENTIERI project, another epidemiological study was conducted in the 55 municipalities in the "Land of Fires." The authors reported increased hospitalization and mortality rates for different types of cancer, such as stomach, liver, lung, bladder, pancreatic, laryngeal, kidney, and breast cancer, and non-Hodgkin's lymphoma in the municipalities of Naples

province.). At the same time, they found significant mortality and hospitalization rates for different types of cancer (stomach, liver, lung, bladder, and laryngeal and leukemia) in the municipality of Caserta provinces^[34] [Table 1].

Another review underlined the association between the high mortality of cancer rate and long-term exposure to toxic wastes^[35] [Table 1]. In 2019, the update of the SENTIERI Project detected an excess of many diseases in people living close to National Priority Contaminated Sites (NPCSs). The methodological approach used in this study did not allow adjusting for several confounding factors being risk factors for the diseases (e.g., smoking, alcohol consumption, obesity). Furthermore, the environmental characterization of the studied NPCSs was not uniform in terms of quality and detection of the pollutants because of the lack of information in different databases. Another limitation of the statistical method was the small population size of many NPCSs and the low frequency of several health outcomes^[36] [Table 1]. However, the authors of this report found an increase in the incidence and mortality of liver, bladder, colorectal, breast, and gastric cancer in Litorale Domizio Flegreo (LDF) (Caserta). In contrast, an increase in mortality rate was observed for liver, bladder, breast, and cervix cancer in Area Litorale Vesuviano (ALV) (Naples)^[36] [Table 1]. Furthermore, they also noted for the first time the health status of children and adolescents (1,160,000 subjects, aged 0–19 years) and young adults (660,000 subjects, aged 20–29 years) in some areas of Campania- Specifically, in AVL, this report showed increased deaths from blood and lymphatic malignancies (in both genders (18 cases; SMR = 156; 90% CI 106–229) and in particular from chronic lymphocytic leukemia in both genders (6 cases; SMR = 210; 90% CI 109–407) among young adults (20–29 years) in comparison to the regional average. Furthermore, an increase in death rate was observed for central nervous system central (CNS) cancers in children aged 0–14 years (6 cases SHR = 140; IC90 = 73–271 between 2006–2013 in comparison to the regional average) and in young adults (0–19 years (7 cases SHE = 129 IC90% = 70–237 between 2006–2013 respect to regional average) with *uncertain data*. In LDF (Caserta Province) and AVL (Naples Province) areas, an increased incidence of non-Hodgkin lymphoma was observed in children aged 0–14 years between 2006–2013 (64 cases; SHR = 137; IC90% 111–168) when compared with a regional average^[36] [Table 1]. Two previous studies reported the number of children affected by different types of cancer in the Campania region^[37,38] [Table 1]. In the first article,^[37] the authors reported the number of cancer cases registered by the AIEOP (Association Italian Pediatric Hematology-Oncology) between 1990–2014 years: 2059 cases in Naples province, 625 cases in Salerno province, 589 in Caserta province, 229 in Avellino province and 153 cases

in Benevento province-37 [Table 1], The authors underlined that the overall ratio between observed (O) and expected (E) was increased during these years^[37] The second article (the EPIKIT study)^[38] [Table 1] found 465 cases of cancers in pediatric age (0–19 years) between 2007 and 2011. In the last decades, a review published in Lancet Oncology reported an increase in incidence of childhood tumors in Europe, especially Italy.^[39] In the sixth report of the ISS published in February 2023)^[40] [Table 1], the authors reported an increase in mortality from all cancers in the LDF area. Additionally, there was evidence between the incidence of breast cancer and the presence of landfills that contained toxic substances such as dioxins and polychlorinated biphenyls. The authors showed increased mortality rates from prostate cancer (680 cases, SMR 116; 90% CI 109–124) and leukemia among males (303 cases, SMR 111; 90% CI 101–122). In addition, the report found a high mortality rate in non-Hodgkin's lymphoma among the female population aged 0–29 years (4 cases, SMR 341; 90% CI 153–760). In female children (aged 0–14), there was an excess of mortality rate for Hemo-lymphopoietic cancers (4 cases, SMR 238; IC90% 107–531). Moreover, in young people (aged 20–29), the mortality rate was increased for CNS cancers (8 cases, SMR 214; IC90% 121–380) and leukemia (SMR 178; IC90% 100–316) in the male population, meanwhile it was noted that there was an excess of the mortality rate of Hodgkin lymphoma in the female population (3 cases, SMR 256; IC90% 102–640). In the end, an increased mortality rate for Hemo-lymphopoietic cancers (in particular Hodgkin lymphoma) was found in both genders and for non-Hodgkin lymphoma in the male population (4 cases, SMR 341; IC90% 153–760) [Table 1]. In the same report, the situation of the ALV area was also described, and the authors underlined the high mortality for breast cancer in females and testis cancer in males. Moreover, in young people, the author found an excess of mortality for lymphoma cancers (10 cases), leukemias (7 cases of lymphoid leukemia, 5 cases), and also for lymphomas 3 cases). They also noted an excess of CNS cancers in pediatric age (among males people: SMR 238; 90% CI 107–529)^[40] [Table 1].

Biomonitoring Analysis in Campania

Since a lot of hazardous waste was illegally burned by releasing dangerous chemicals (such as 2,3,7,8-tetracas lhorodibenzo-p-dioxins-TCDD) in the Campania region, several studies were carried out to better understand the link between waste-related pollution and biomarkers assessment in humans, by using different approaches. A study was conducted on amniotic fluid samples derived from women living close to toxic sites in Campania (in the north-east Naples area and compared with control samples of women who lived in non-polluted areas (Avellino, Campania). The

authors evaluated the genetic impact of these amniotic fluids on *Paracentrotus lividus* embryos. They observed DNA damage through RAPD (Random Amplified Polymorphism DNA) profiles only in embryos exposed to samples derived from women living in polluted areas. Using this method, they found two target regions for DNA alterations in the genome of *Paracentrotus lividus*.^[41] Another study found that PCDD/Fs and PCB serum levels in the population of the Naples area were low when compared with those of populations living in exposed areas.^[42] On the contrary, a study conducted by De Felice *et al.* reported that pregnant women living in reported that pregnant women living polluted waste landfill sites had shorter telomerases than pregnant women living in non-polluted area.^[43] Moreover, Rivezzi *et al.*^[44] analyzed milk samples derived from 94 primiparas living in municipalities of the provinces of Naples and Caserta. They found a significant correlation with the age of sampled women, illegal waste fires, and environmental dioxin risk index (EDR).^[44] Similarly, another article reported the high dioxin levels in the breast milk of mothers living in Naples and Caserta provinces. In this case, the authors reported a positive correlation between the age of mothers and a high concentration of PCDDs/Fs and PCBs in their milk.^[45] Furthermore, the SEBIOREC (Studio Epidemiologico Biomonitoraggio Regione Campania) study reported biomarkers' levels in the Campania region per European and Italian values, except for some pollutants (arsenic, mercury, dioxins) detected in four municipalities of Naples.^[46] In accordance with these data, in another study, the authors analyzed the levels of polychlorinated dibenzo-p-dioxins, polychlorinated dibenzofurans, and polychlorinated biphenyls in blood sample derived from donors living in area of Naples city and its province Acerra, Nola, Marigliano (high polluted area) and Pompei, Portici, Pozzuoli, Torre del Greco. The concentrations of the pollutants were almost the same in both people living in polluted areas (Acerra, Nola Marigliano) and those living in low polluted areas (including Naples city, Pompei, Portici, Pozzuoli, Torre del Greco).^[47] Furthermore, Bergamo *et al.*^[48] a pilot study (EcoFoodFertility initiative) was carried out on human semen in 110 healthy males living in two different areas of Campania: one with high and another with low environmental pressure. The authors found that the population living in areas had high levels of zinc, copper, chromium, and decreased iron levels. Additionally, there was reduced sperm motility and higher sperm DNA Fragmentation Index (DFI) in the semen of men. Another pilot biomonitoring study was carried out in 112 clinically healthy, normospermic men living in different locations of the Campania region with high or low environmental impact on telomere length (TL) in both leukocytes (LTL) and sperm cells (STL). In this study, the authors found that telomeres were longer in sperm cells derived from young people living

in highly polluted areas than that of young people living in polluted regions.^[49]

DISCUSSION

The illegal dumping of hazardous waste materials is a major global issue impacting human health. Many studies reported the strong impact of toxic waste on human health because it can contain high levels of contaminants involved in several disease outcomes. For example, toxic substances can induce cancers after long latency periods. For this reason, it can be challenging to establish in a population that excess cancers can be due to land contamination. Moreover, many epidemiological studies have been conducted to better understand the relationship between toxic waste and its impact on human health. The results of these studies can raise some concerns. Firstly or Primarily, the associations identified between mortality and environmental pressure from waste are often fragile, and secondly, the lack of data on exposure levels can make it challenging to evaluate health effects arising from exposure to waste, which is not always incremental with respect to the increase in exposure. Oncological mortality cannot be considered a risk index since many variables can intervene and modify the path from diagnosis to recovery or death. Two studies^[50,51] used a synthetic index by considering the distance from dumping sites, specific characterization of the waste disposal, population percentage living close to these areas, and finally, the characterization of neighboring areas through geographic information system (GIS). In this study, the authors underlined low statistical association among results. In addition, few data are provided by the Cancer Registry of Local Health Authority "Naples 4," and the National Hospital Discharge Records database, the National Bureau of Statistics (ISTAT). In this context, in Campania, the principal issues are locating all illegal waste dumping sites and identifying the population at risk to find the potential health effects related to waste exposure. Creating a network of expertise to develop a real-time environmental monitoring solution using integrated technology to access environmental data for risk identification should be necessary to reduce environmental risks. Epidemiological surveillance in contaminated areas of Campania could play a crucial role in monitoring health status changes related to environmental contamination through modern methodologies and credible information. In this perspective, different projects are carried out to better characterize this situation in Campania. The Experimental Zooprophyllactic Institute of Southern Italy (IZSM), in collaboration with the Terra dei Fuochi working group, is carrying out surveys both on food (QR Code Campania project^[51]) and on the environment (Campania Trasparente project^[52]) using a mathematical model that can estimate a synthetic index of environmental pressure

at a municipality level (Municipality Environmental Pressure Index – MEPI).^[53] In this project, the analysis of environmental and biological samples (including soil air and human blood specimens) will be performed. Furthermore, a new biomonitoring model^[54] will be based on a new analytical evaluation of the environmental context to identify the pollution source, the migration pathways of those pollutants, and their effects on target organisms. This project will include 4205 residents of the Campania region who are enrolled in the Studio di Esposizione nella Popolazione Suscettibile “SPES” (Study of Exposure in Susceptible Population) biomonitoring study, which predominantly focused on the areas dubbed “Land of Fires” in the recent decades. The cooperation among epidemiologists, biologists, environmentalists, and regulatory agencies must occur at local and state levels to support these projects.

CONCLUSION

In summary, it will be important:

1. To establish commissions of experts to identify a “sustainable” system for the disposal of waste to decrease the pollution and to avoid environmental degradation and decrease the risk of different types of cancer and high costs for the community.
2. To *requalify* and redevelop contaminated areas.
3. To increase penalties for environmental crimes.
4. To allocate funds confiscated from organized crime for reclamations of contaminated areas.

Authors’ contributions

Gabriella Marfe and stefania Perna conceived and planned the project. Gabriella Marfe, Stefania Perna and Giovanna Mirone participated in the study design in developing methods for data collection and analysis - All authors contributed to the refinement of the study protocol and approved the final manuscript.

Ethical approval

The Institutional Review Board approval is not required.

Declaration of patient consent

Patient’s consent is not required as there are no patients in this study.

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Conflicts of interest

There are no conflicts of interest.

Use of artificial intelligence (AI)-assisted technology for manuscript preparation

The authors confirm that there was no use of artificial intelligence (AI)-assisted technology for assisting in the writing or editing of the manuscript and no images were manipulated using AI.

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