# Cancer mortality and congenital anomalies in a region of Italy with intense environmental pressure due to waste

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## ABSTRACT

**Objectives:** Waste management in the Campania region has been characterised, since the 1980s, by widespread uncontrolled and illegal practices of waste dumping, generating concerns over the health implications. The objective of this study was to evaluate possible adverse health effects of such environmental pressure.

**Methods:** The health effects of waste-related environmental exposures in Campania were assessed in a correlation study on nine causes of death (for the years 1994–2001) and 12 types of congenital anomaly (CA) (1996–2002) in 196 municipalities of the provinces of Naples and Caserta. Poisson regression was used to analyse the association between health outcomes and environmental contamination due to waste, as measured through a composite index, adjusting for deprivation.

**Results:** Statistically significant excess relative risks (ERR, %) in high-index compared with low-index (unexposed) municipalities were found for all-cause mortality (9.2 (95% CI 6.5 to 11.9) in men and 12.4 (9.5 to 15.4) in women and liver cancer (19.3 (1.4 to 40.3) in men and 29.1 (7.6 to 54.8) in women). Increased risks were also found for all cancer mortality (both sexes), stomach and lung cancer (in men). Statistically significant ERRs were found for CAs of the internal urogenital system (82.7 (25.6 to 155.7)) and of the central nervous system (83.5 (24.7 to 169.9)).

**Conclusion:** Although the causal nature of the association is uncertain, findings support the hypothesis that waste-related environmental exposures in Campania produce increased risks of mortality and, to a lesser extent, CAs.

The health impact of waste management and disposal has been studied in many settings, and findings of several studies have been reviewed.[1–4] Landfilling, one of the main methods of waste disposal and focus of this study, has been repeatedly investigated as a potential risk factor for a variety of health outcomes, including mortality and morbidity,[5–7] reproductive endpoints[8–11] and measures of perceived health and wellbeing.[12–15] Overall, the evidence is not conclusive of a clear role of landfilling as a vehicle of exposures with established health effects. However, several positive associations have been observed and, importantly, high proportions of people may be affected in industrialised countries, for example, 80% of residents in the UK are known to live within 2 km of one or more landfills.[5 8] Thus the exposures caused by landfills may have high prevalence in the general population, potentially turning small risks, if confirmed, into non-negligible public health impacts.

Most of the available studies were carried out in reasonably controlled settings, that is, where waste disposal is managed applying relatively tight and regulated practices, aiming at minimising releases of toxic agents through air, soil and water contamination (occupational exposures are not considered in this article). Less is known of the health effects of waste-related exposures in settings with lower standards of waste management practices, such as the case of Campania, a region of southern Italy known for its problematic waste situation. The northern part of the region, consisting of two of the five provinces, Naples and Caserta (illustrated in fig 1), has frequently been in the news, over the last 15–20 years, because of the periodic crises in public-run waste collection services. Well-known operations have also been run, since the early 1980s, by organised crime cartels, resulting in documented practices of illegal dumping and open-air burning of urban and toxic waste.[16] Waste management in the whole Campania region has been run under a central government-declared emergency regime since 1994. In short, a difficult to quantify but large proportion of waste produced in the region, plus waste transferred into the region by organised crime, has been illegally disposed of and burned for some two decades.

A major reason of concern, of increasing prominence in the often controversial public debate, has regarded the health effects of such practices. Acute effects, such as the possible outbreak of vector-borne infections and general safety issues, are of obvious concern, but possible long-term health effects also attract much attention, given the protracted emergency status. A first reportage suggested increased occurrence of cancer mortality and identified a so-called ''triangle of death''[17] within the area, where mortality was elevated and claimed to be attributable to waste-related exposures. Subsequently, descriptive studies on cancer mortality and congenital anomalies[18 19] confirmed the presence of marked excesses mostly in the same areas, but the geographical pattern was found to be more complex and, more importantly, suggested that the possible role of waste must be considered together with that of other strong determinants, such as socioeconomic status, nutrition, primary care and infections. There was also a visual correlation between the spatial pattern of mortality and malformation risks and that of highest concentration of known waste dumping sites, with a tendency for the excesses to cluster in the area around the boundary between

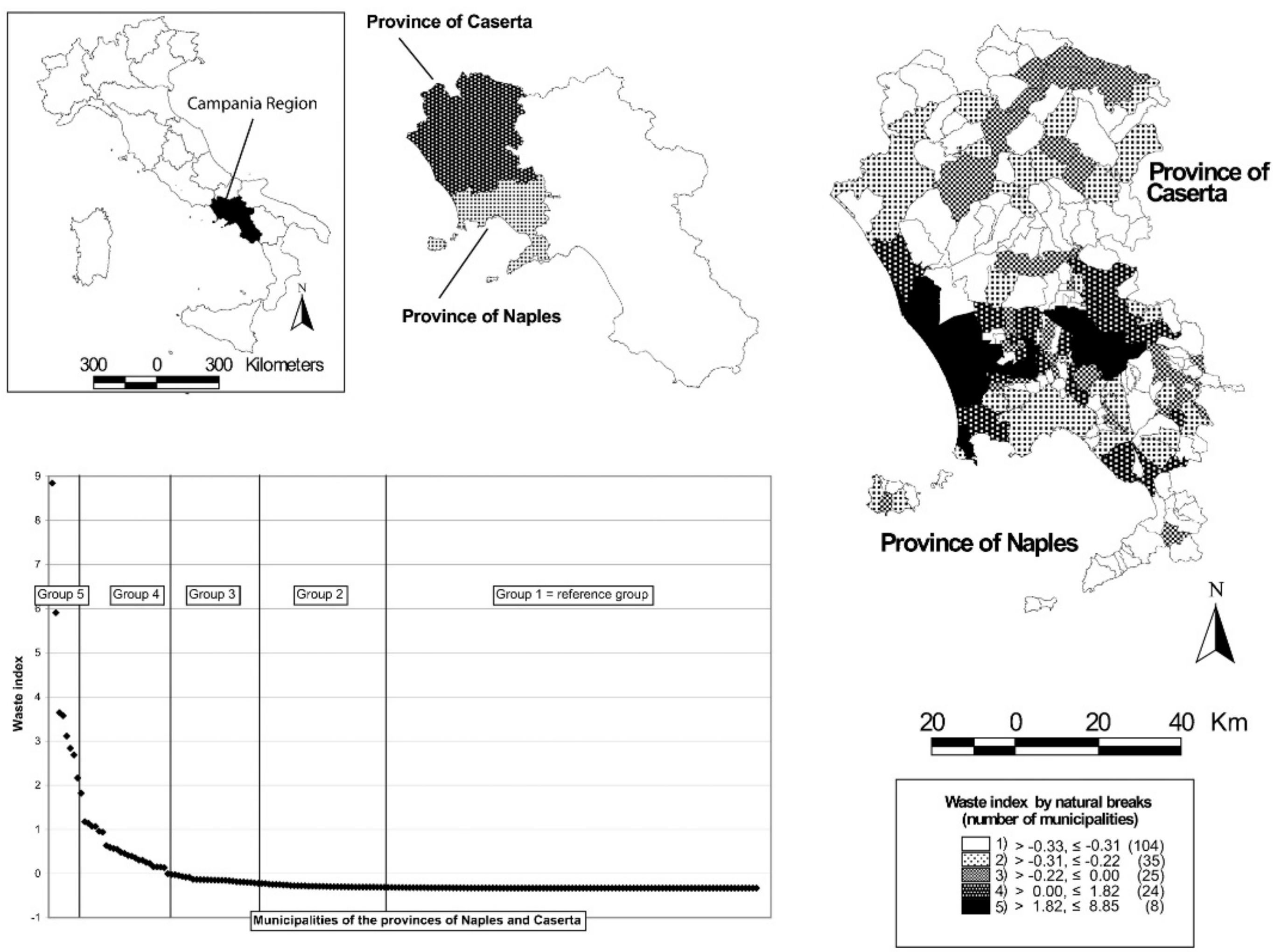


**Figure 1** Distribution of the waste index in the 196 municipalities of the provinces of Naples and Caserta.

the two provinces of Naples and Caserta and along the Tyrrhenian coast of Caserta province. However, no formal analysis of the correlation between health outcomes and waste exposures was made, as exposure data had not been assembled. The present study was thus motivated by the need to measure such association, using existing health data and an approximate but systematic measure of the waste-related exposures, as was carried out in other settings,[20 21] and trying to account for other known risk factors.

## MATERIALS AND METHODS

This study evaluates the hypothesis that in the two provinces of Naples and Caserta overall mortality, cancer mortality and occurrence of congenital anomalies are spatially correlated with the intensity of legal and illegal landfills and waste dumping sites. The unit of analysis consists of the 196 municipalities comprised in the two provinces. Mortality data were retrieved from the Italian National Institute of Statistics for 1994–2001; specific death causes (table 1; supplementary online material) were selected on the basis of the published literature on the health effects of waste-related exposures.

Congenital anomalies data, regarding live births, stillbirths and termination of pregnancy, were obtained from the Campania region registry of congenital anomalies (a full member of the European network for surveillance of congenital anomalies (EUROCAT) and part of the International Clearinghouse for Birth Defects and Surveillance and Research (ICBDSR)) for 1996–2002, and were grouped by subtypes (table 1; supplementary online material), following standard classification. Yearly population data from the Italian National Institute of Statistics (ISTAT) were used as denominators: number of residents for mortality and number of resident total births for congenital anomalies. Using number of births from ISTAT as denominators, rather than from the congenital anomalies registry, was necessary because registry data on births do not include the residence municipality.

Data from the 1991 census were used to calculate a deprivation index at municipality level, applying an established methodology based on variables on education, unemployment, housing ownership, surface of the dwelling, and family structure.[22] The 1991 census data were preferred to the 2001 data to allow for long latencies for cancer mortality, and used in all analyses also considering the high correlation between the two indices (correlation coefficient = 0.85). Municipalities were subdivided in quintiles with respect to the value of the deprivation index (1 = least deprived; 5 = most deprived).

The degree of environmental pressure due to waste dumping activities was estimated through the creation of a synthetic index, used at municipality level.[23 24]

A database with over 300 waste landfilling or dumping sites, built by the regional Environmental Protection Agency, was used. This database included both authorised landfills and illegal waste dumping sites. Two hundred and twenty-seven sites were selected for the analysis (89 legal and 138 illegal) if: (1) hazardous wastes were present; or (2) total waste volume was more than 10 000 $m^3$. A group of independent experts then evaluated each selected site in terms of its potential hazard, assessed on the basis of the likelihood of releases on water, soil and air. Sites were grouped into seven categories of decreasing hazard, as shown in table A1 in the Appendix.[23] A 1 km-radius circle was drawn in a Geographic Information System around the centre of each site; the study area was thus partitioned into zones according to the presence of these circles (yes or no, number of overlapping circles) and their intersections. The choice of a 1 km radius, smaller than what has been used in some comparable studies,[8 9] was motivated by the high density of the waste sites in the study area and the frequent overlap of the circles, and by the high population density, which guarantees high statistical power. Data on population counts by census tract (a geographical unit smaller than municipality, with 20 (median value) tracts per municipality) were combined with the ordinal classification of the zones, producing a value of population-weighted intensity of waste-related exposure. Each of the 196 municipalities was then given a summary index, resulting from summing the scores of all the zones comprised in the municipality. The ranking scale was designed in such a way that the presence of multiple low-hazard sites in one area, produces a lower score than one of the high-hazard sites. Finally, municipalities were categorised in five groups, using so-called natural breaks, that is, cut points that maximise homogeneity within groups and heterogeneity between groups.[25] Distribution of the index by municipality and geographical distribution are shown in fig 1.

The correlation analysis between the health endpoints, the waste index and the deprivation index was carried out applying standard Poisson regression models, using the STATA software package. All mortality models included age (in 5-year groups except for the first group of 0–14 years of age); for both mortality and congenital anomalies models, the five groups defined by the deprivation index and the waste index were used as categorical factors in the analysis; linear trends were also estimated across the five groups of both indices, by coding the categories from 1 to 5, and taking these codes as quantitative figures. A variable for time period was also included, but subsequently discarded from the regression models given the lack of any effect. All mortality analyses were carried out separately for men and women, due to different patterns of occupational exposures and different mortality rates for some endpoints.

A hierarchical Bayesian conditional autoregressive normal model, including terms for spatially unstructured and spatially structured effects[26 27] was also fitted, using the WinBUGS software, in order to evaluate the sensitivity of the risk estimates to extra-Poisson variability and spatial autocorrelation.

## RESULTS

The 196 municipalities had a population (average over 1994–2001) of 1 921 315 men and 2 023 954 women. There were, respectively, 123 627 and 116 872 deaths, in total in 1994–2001. A total of 4192 cases with congenital anomalies were registered out of 351 416 total births in 1996–2002. The classification of municipalities in groups by index of waste-related environmental pressure produced a skewed distribution with 8, 24, 25, 35 and 104 municipalities, respectively, in the five classes, from most exposed to least exposed, the latter being taken as reference group (see fig 1). Table 1 gives the details on population and mortality, including the causes of death studied, by the five levels of exposure (''exposure'' henceforth refers to the summary index described above); table 2 gives the details on births and congenital anomalies.

Tables 3 and 4 present the results of the regression analysis. For mortality, statistically significant trends were found for all-cause mortality in men and women; statistically significant or borderline significant trends were also found for all cancers, liver cancer in both sexes, lung cancer in men, and stomach cancer in men. These trends reflect marked differences between the different groups of municipalities; using the group with lowest exposure as reference, excess relative risk estimates in the highest group are, for example, 9.2 and 12.4% for men and women, respectively, 4.1 and 6.6% for all cancer mortality, and 19.3 and 29.1% for liver cancer mortality. No association was detected between the waste index and mortality from the pool of all cancers other than those individually analysed.

For congenital anomalies, association is less marked, with only two significant trends observed: one positive for congenital anomalies of the internal urogenital system and one negative for cardiovascular anomalies. Comparisons between high exposure municipalities (group 5) with reference (group 1) were statistically significant for congenital anomalies of the internal urogenital system (82.7%) and for congenital anomalies of the central nervous system (83.5%).

These risks are adjusted for deprivation, which was associated with the waste index (correlation = 0.30). As expected, the deprivation index was significantly associated with most mortality endpoints, for both sexes (see table 3), with significant trends of increasing overall mortality across deprivation quintiles; positive associations were obtained for all cancer mortality, lung cancer, liver cancer and kidney cancer in both sexes, bladder cancer and non-Hodgkin lymphoma in men only; associations were null or non-significant for stomach cancer and soft tissue sarcoma in both sexes and, for women, non-Hodgkin lymphoma; for all other cancers combined, significant associations were found for men and women.

Association between deprivation and risk of congenital anomalies was also found; the trend was statistically significant for all anomalies combined ($p<0.001$), cardiovascular anomalies ($p<0.001$), and limb anomalies ($p = 0.013$). For the other types of anomaly, associations were null or non-significant.

The analysis carried out with hierarchical Bayesian modelling is available in tables 2 and 3 in the supplementary online material. Results are robust with a comparable overall pattern, and little deviation suggesting limited extra-Poisson variability (spatially structured and unstructured). The one notable exception, however, was the risk estimate for all congenital anomalies combined: excess relative risks in all exposure levels, compared with the reference unexposed group were positive, although not statistically significant (11.2, 10.5, 10.5, 29.1% in groups 2 to 5, respectively).

## DISCUSSION

The intensity of waste-related exposure, as measured by the summary index based on density and degree of hazard of known waste disposal sites, correlates with the occurrence of several health endpoints, among those selected for this study. At municipality level, total mortality, all cancer mortality, and mortality from some specific cancer sites have increasing risks, for one or both genders, by increasing exposure, with statistically significant linear trends across five exposure groups. Trends are significant in five of nine causes of death in men, and

**Table 1** Population and mortality (1994–2001) by gender and waste index category in Naples and Caserta provinces

| Waste index | Municipalities | Average population | All-cause mortality | Cancer mortality | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | Total | Lung | Liver | Stomach | Bladder | Kidney | STS | NHL | Other cancers |
| Men | | | | | | | | | | | | |
| I group | 104 | 546956 | 34079 | 10271 | 3321 | 674 | 664 | 592 | 182 | 38 | 218 | 4582 |
| II group | 35 | 739897 | 53106 | 15989 | 5267 | 953 | 933 | 1000 | 270 | 59 | 381 | 7126 |
| III group | 25 | 133758 | 7853 | 2297 | 751 | 165 | 144 | 112 | 38 | 8 | 63 | 1016 |
| IV group | 24 | 345503 | 20130 | 6261 | 2065 | 404 | 433 | 356 | 94 | 17 | 149 | 2743 |
| V group | 8 | 155201 | 8459 | 2525 | 843 | 204 | 171 | 130 | 38 | 11 | 53 | 1075 |
| **Total** | **196** | **1921315** | **123627** | **37343** | **12247** | **2400** | **2345** | **2190** | **622** | **133** | **864** | **16542** |
| Women | | | | | | | | | | | | |
| I group | 104 | 575379 | 31854 | 6783 | 471 | 546 | 427 | 113 | 91 | 16 | 210 | 4909 |
| II group | 35 | 791123 | 52167 | 11435 | 1178 | 816 | 608 | 212 | 167 | 59 | 351 | 8044 |
| III group | 25 | 139357 | 7124 | 1490 | 112 | 122 | 89 | 22 | 20 | 8 | 47 | 1070 |
| IV group | 24 | 358155 | 18226 | 4038 | 301 | 342 | 239 | 63 | 55 | 17 | 137 | 2884 |
| V group | 8 | 159939 | 7501 | 1639 | 128 | 163 | 102 | 19 | 27 | 11 | 46 | 1143 |
| **Total** | **196** | **2023954** | **116872** | **25385** | **2190** | **1989** | **1465** | **429** | **360** | **111** | **791** | **18050** |

NHL, non-Hodgkin lymphoma; STS, soft tissue sarcoma.

**Table 2** Births and congenital anomalies (1996–2002) by waste index category in Naples and Caserta provinces

| | | | Congenital anomalies | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Waste index | Municipalities | Total births | Total | Nervous system | Neural tube defect | CVD | Orofacial clefts | Digestive system | External genital system | Hypospadias | Internal urogenital system | Musculoskeletal and connective tissue | Limbs | Chromosomal |
| I group | 104 | 99293 | 1100 | 81 | 38 | 326 | 64 | 51 | 99 | 87 | 82 | 52 | 167 | 92 |
| II group | 35 | 127392 | 1643 | 133 | 56 | 476 | 91 | 63 | 147 | 139 | 137 | 82 | 219 | 188 |
| III group | 25 | 25476 | 326 | 34 | 14 | 93 | 15 | 10 | 37 | 31 | 28 | 13 | 42 | 33 |
| IV group | 24 | 65320 | 712 | 54 | 23 | 189 | 50 | 32 | 59 | 57 | 86 | 33 | 109 | 55 |
| V group | 8 | 33935 | 411 | 46 | 16 | 106 | 23 | 11 | 32 | 29 | 49 | 22 | 56 | 31 |
| **Total** | **196** | **351416** | **4192** | **348** | **147** | **1190** | **243** | **167** | **374** | **343** | **382** | **202** | **593** | **399** |

CVD, cardiovascular.

**Table 3** Excess percentage of relative risks for mortality by gender, waste index category and deprivation index*

| Excess risks | | | | | | | |
|---|---|---|---|---|---|---|---|
| | By waste index group | | | | | | By deprivation index group |
| *Cause of death – men* | *I* | *II (95% CI)* | *III (95% CI)* | *IV (95% CI)* | *V (95% CI)* | *Trend (95% CI)* | *Trend (95% CI)* |
| All causes | 1 | **5.4† (3.7 to 7.2)** | **7.9 (5.2 to 10.7)** | **3.9 (2 to 5.9)** | **9.2 (6.5 to 11.9)** | **1.7 (1.2 to 2.2)** | **3.0 (2.6 to 3.4)** |
| All cancers | 1 | **4.2 (1.1 to 7.5)** | **5.6 (0.8 to 10.6)** | **4.9 (1.3 to 8.5)** | 4.1 (−0.5 to 8.9) | **1.5 (0.6 to 2.3)** | **4.4 (3.6 to 5.2)** |
| Lung cancer | 1 | **5.5 (0 to 11.2)** | 6.4 (−2 to 15.4) | 6.1 (−0.1 to 12.7) | 6.7 (−1.3 to 15.4) | **1.9 (0.4 to 3.3)** | **4.9 (3.4 to 6.4)** |
| Liver cancer | 1 | −9.2 (−19.5 to 2.4) | **20.6 (1.2 to 43.8)** | 0.7 (−12.1 to 15.3) | **19.3 (1.4 to 40.3)** | **4.3 (1 to 7.7)** | **8.2 (4.7 to 11.7)** |
| Stomach cancer | 1 | 3.0 (−8.7 to 16.2) | 2.8 (−14.5 to 23.7) | **19.4 (4.5 to 36.4)** | 15.7 (−2.9 to 37.7) | **5.2 (1.8 to 8.7)** | −1.3 (−4.2 to 1.8) |
| Bladder cancer | 1 | 11.7 (−1.6 to 26.8) | −6.4 (−23.9 to 15.2) | 7.1 (−7.4 to 23.9) | −4.1 (−21.2 to 16.6) | −0.7 (−4.1 to 2.9) | **8.3 (4.7 to 12.0)** |
| Kidney cancer | 1 | −2.8 (−23 to 22.6) | −0.6 (−30.7 to 42.5) | −14.9 (−35.2 to 11.7) | −16.7 (−41.9 to 19.4) | −4.0 (−10.2 to 2.6) | 6.2 (−0.3 to 13 |
| Soft tissue sarcoma | 1 | −9.8 (−44.6 to 46.9) | −20.4 (−63.3 to 72.6) | −31.0 (−63 to 29) | 25.0 (−38.8 to 155.1) | −3.9 (−16.5 to 10.7) | 4.7 (−9.0 to 20.0) |
| Non-Hodgkin lymphoma | 1 | 9.4 (−10.3 to 33.4) | 25.4 (−6 to 67.4) | 6.8 (−15 to 34.1) | −3.7 (−29.4 to 31.4) | 1.3 (−4 to 7) | **5.7 (0.2 to 11.5)** |
| Other cancers | 1 | **4.7 (0 to 9.6)** | 4.3 (−2.8 to 11.8) | 3.3 (−2 to 8.9) | 0.3 (−6.4 to 7.5) | 0.7 (−0.01 to 2) | **3.7 (2.5 to 5.0)** |
| *Cause of death – women* | *I* | *II (95% CI)* | *III (95% CI)* | *IV (95% CI)* | *V (95% CI)* | *Trend (95% CI)* | *Trend (95% CI)* |
| All causes | 1 | 1.7 (−0.1 to 3.5) | **8.1 (5.3 to 11)** | **4.8 (2.7 to 6.9)** | **12.4 (9.5 to 15.4)** | **2.4 (1.9 to 2.9)** | **1.2 (0.7 to 1.6)** |
| All cancers | 1 | **5.1 (1.3 to 9.1)** | 2.4 (−3.3 to 8.5) | 3.6 (−0.8 to 8.1) | **6.6 (0.8 to 12.7)** | **1.0 (0 to 2.1)** | **3.4 (2.4 to 4.4)** |
| Lung cancer | 1 | **45.4 (27.5 to 65.9)** | 14.4 (−7.5 to 41.5) | 5.6 (−9.8 to 23.6) | 9.4 (−10.5 to 33.8) | −2.3 (−5.7 to 1.3) | **16.8 (12.6 to 21.2)** |
| Liver cancer | 1 | −9.3 (−20.6 to 3.6) | 9.1 (−10.9 to 33.6) | 9.6 (−5.6 to 27.2) | **29.1 (7.6 to 54.8)** | **6.6 (2.8 to 10.5)** | **4.7 (1.1 to 8.5)** |
| Stomach cancer | 1 | −8.3 (−21.2 to 6.8) | −6.4 (−26 to 18.2) | 2.2 (−14.2 to 21.7) | 16.7 (−6.9 to 46.2) | 2.6 (−1.7 to 7) | −2.8 (−6.5 to 1.0) |
| Bladder cancer | 1 | 7.7 (−19.3 to 43.7) | −12.7 (−45.3 to 39.4) | −2.8 (−30.9 to 36.7) | −16.7 (−49.6 to 37.7) | −3.3 (−11 to 5) | 3.1 (−4.3 to 11.0) |
| Kidney cancer | 1 | 6.9 (−22.2 to 46.9) | 11.2 (−32.5 to 83.1) | 3.4 (−28.5 to 49.5) | 19.1 (−23.7 to 86) | 1.7 (−6.7 to 10.9) | **14.0 (4.3 to 24.5)** |
| Soft tissue sarcoma | 1 | 7.7 (−38.9 to 89.8) | 84.1 (−11.3 to 282) | 33.6 (−27.4 to 145.9) | −0.3 (−57.4 to 133.7) | 8.3 (−6.5 to 25.4) | −3.2 (−15.9 to 11.5) |
| Non-Hodgkin lymphoma | 1 | 10.1 (−10.8 to 35.7) | 3.5 (−25.2 to 43.2) | 19.7 (−5.7 to 52) | −0.2 (−28.3 to 39) | 1.6 (−4.1 to 7.6) | 1.8 (−3.6 to 7.5) |
| Other cancers | 1 | 3.5 (−0.01 to 8.2) | 1 (−5.7 to 8.1) | 2.3 (−2.8 to 7.6) | 3.7 (−3 to 10.8) | 0.7 (−0.01 to 1.9) | **2.3 (1.2 to 3.5)** |

*Relative risks for waste index and for socioeconomic deprivation index are mutually adjusted.
†In bold, statistically significant relative risks are reported.

**Table 4** Excess percentage of relative risks for congenital anomalies (CAs) by waste index category and deprivation index*

| Excess risks | | | | | | | |
|---|---|---|---|---|---|---|---|
| | By waste index group | | | | | | By deprivation index group |
| CAs | I | II (95% CI) | III (95% CI) | IV (95% CI) | V (95% CI) | Trend (95% CI) | Trend (95% CI) |
| All CAs | 1 | 8.7 (−0.2 to 18.3) | **14.0† (0.5 to 29.4)** | −7.3 (−16.2 to 2.5) | 5.2 (−6.5 to 18.4) | −1.0 (−3.2 to 1.4) | **5.5 (2.8 to 8.2)** |
| CAs of the nervous system | 1 | 21.9 (−10.1 to 65.3) | 45.1 (−3.6 to 118.5) | −3.3 (−33 to 39.6) | **83.5 (24.7 to 169.9)** | 7.5 (−0.04 to 16.3) | −3.9 (−11.7 to 4.6) |
| Neural tube defect | 1 | 9.0 (−31.1 to 72.6) | 21.7 (−34.8 to 127.1) | −10.5 (−48.7 to 56.4) | 45.3 (−22.1 to 171.1) | 2.4 (−9.4 to 15.7) | −5.9 (−17.2 to 6.9) |
| Cardiovascular anomalies | 1 | 3.9 (−11.2 to 21.7) | 15.8 (−8.6 to 46.8) | **−17.4 (−31.8 to −0.1)** | −13.9 (−31.3 to 8) | **−5.3 (−9.4 to −1)** | **12.5 (6.9 to 18.4)** |
| Orofacial clefts | 1 | 18.1 (−17.4 to 68.8) | −2.6 (−45.3 to 73.4) | 18.7 (−20.1 to 76.5) | −2.1 (−40.2 to 60.3) | 2.5 (−6.8 to 12.7) | −0.3 (−10.1 to 10.6) |
| CAs of the digestive system | 1 | −8.7 (−39.8 to 38.4) | −23.4 (−61.7 to 53.4) | −13.5 (−46.2 to 38.9) | −42.2 (−70.4 to 12.8) | −7.0 (−17.5 to 4.8) | 2.9 (−9.4 to 16.9) |
| CAs of the external genital system | 1 | 3.8 (−21.9 to 37.9) | 39.6 (−5.3 to 105.9) | −17.0 (−41.2 to 17) | −8.9 (−39.7 to 37.8) | −3.4 (−10.7 to 4.5) | 5.6 (−3.2 to 15.2) |
| Hypospadias | 1 | 15.8 (−14.1 to 56.2) | 36.8 (−10.3 to 108.5) | −5.7 (−34 to 34.7) | −6.2 (−39.4 to 44.9) | −2.6 (−10.2 to 5.7) | 6.3 (−2.9 to 16.5) |
| CAs of the internal urogenital system | 1 | 23.4 (−8.5 to 66.4) | 25.6 (−18.9 to 94.5) | **53.7 (11 to 112.9)** | **82.7 (25.6 to 165.7)** | **13.8 (5.8 to 22.5)** | 1.1 (−7.1 to 10.0) |
| Musculoskeletal and connective tissue CAs | 1 | 24.6 (−15.2 to 83.1) | −10.3 (−51.6 to 66.4) | −0.4 (−37.6 to 59) | 41.6 (−16.6 to 140.2) | 1.1 (−9 to 12.2) | −3.4 (−13.5 to 8.0) |
| CAs of the limbs | 1 | −8.1 (−26.6 to 15.1) | −1.0 (−30 to 40) | −9.7 (−30.3 to 17) | −10.6 (−34.7 to 22.3) | −2.0 (−7.9 to 4.3) | **9.4 (1.9 to 17.4)** |
| Chromosomal CAs | 1 | **51.6 (14.8 to 100.2)** | 38.6 (−7.9 to 108.5) | −11.3 (−37.7 to 26.4) | −2.8 (−36.3 to 48.1) | −6.4 (−13.4 to 1.1) | 8.8 (−0.1 to 18.6) |

*Relative risks for waste index and for socioeconomic deprivation index are mutually adjusted.
†In bold, statistically significant relative risks are reported.

three of nine in women, largely above what could be expected by chance due to multiple testing under the null hypothesis of no association (at the 5% significance level, 0.9 significant trends are expected by chance alone). Congenital anomalies are less markedly associated with exposure, with one significant increasing trend (for anomalies of the internal urogenital system) and one significant decreasing trend (for cardiovascular anomalies) out of 12 tested. For another type of anomaly, congenital anomalies of the central nervous system, the trend is not significant, but a significant excess risk, based on 46 cases, was observed in the most exposed group. All anomalies combined are not associated with exposure in the standard Poisson regression analysis, but are in the Bayesian analysis, where extra-Poisson variability and spatial autocorrelation are taken into account.

These results cannot be easily compared with those of other multi-site studies on landfills and health, because of the marked differences in the settings. For example, the UK studies on cancer incidence[5] and the EUROHAZCON study on congenital anomalies[9] address the residential risk due to living in the vicinity of known legal and controlled landfill sites, as opposed to the widespread occurrence of illegal sites of highly variable characteristics. This lack of comparability with previous studies makes causal inference all the more challenging. Several questions must be addressed when evaluating the nature of the associations. Data quality in the study area, for mortality, is in line with national figures, with proportions of ill-defined deaths ranging from 1.2 to 3% in the two provinces, for men and women. Some caution is needed, on the other hand, for congenital anomalies, given a coverage of approximately 75% of all deliveries, due to the fact that some maternity units did not provide delivery data to the regional registry in the study period.[28]

Exposure data are based on the available database of sites of legal and illegal waste dumping. While this database is quite detailed, the very nature of illegal waste dumping operations is almost certain to produce some degree of incompleteness of the data, and a non-systematic undercoverage of illegal dump sites. This in turn may result in some error in estimating the exposure index at municipality level, with uncertain consequences on risk estimates.

All models used in the analysis included a municipality-level deprivation index, used for controlling the possible confounding effect of socioeconomic variables. The index has been used in correlation studies in Italy and its effectiveness in removing confounding has been documented.[29] Results from this study suggest an important role of socioeconomic factors, and the need to control for them in this kind of analysis. However, it is possible, also in consideration of the ecological study design, that residual confounding, not captured by the deprivation index, may be present and explain part of the associations found for waste exposure. Other risk factors that may partially explain the associations include determinants such as quality of primary care, lifestyle, tobacco consumption, hepatitis infections and other kinds of environmental degradation, for which systematic data are not available in the study area. Hepatitis infection, in particular, shows an elevated prevalence in the study area.[30 31] This might produce possible confounding on mortality from liver cancer; however, the possibility of interaction between hepatitis virus and hepatotoxic carcinogenic chemicals should be considered, if these chemicals have a fibrogenic action, as in the case of vinyl chloride.[32] In more general terms, while some of the risk factors mentioned above are likely to be more powerful health determinants than waste-related exposures, there are no obvious reasons (perhaps other than socioeconomic factors) why they should correlate, at the municipality level, with intensity of waste dumping and thus produce a positive confounding effect.

Conversely, some factors are supportive of a causal role of waste-related exposures on the health outcomes under study. The different analyses have a certain internal consistency, with regards to: a relatively large number of positive and significant risk estimates, and only one negative (that may be due to multiple comparison); comparability of risks in men and women; coherent behaviour of estimates when adjusting for deprivation index (the estimates were reduced); absence of association between the waste index and all cancers other than those selected a priori for the analysis, combined; and robustness of models when allowing for extra-Poisson variability (spatially structured and unstructured). Positive associations were found for outcomes with long latency times, such as lung cancer mortality, and for one outcome with latency of less than 1 year (internal urogenital congenital anomalies), consistently with the fact that waste mismanagement has been a problem in the area for at least two decades, and that waste dumping sites established and used in the past have not yet been cleaned up.[16]

Thus, on balance, factors suggestive of a role of waste-related exposures as a contributory causal component of the association are somewhat stronger than those suggestive of an artefact. The overall picture, though not clear, is in fact compatible with the occurrence of adverse health effects of intense environmental pressure due to waste disposal practices in Campania. Validating this observation may be difficult, as no systematic environmental monitoring has so far taken place in the area, and only sporadic ad hoc measurements have been performed, aimed at documenting highly polluted spots, of particular interest for local environmental remediation or for criminal prosecution. In these measurements, a range of chemical agents, namely heavy metals, polychlorinated biphenyls, dioxins and polycyclic aromatic hydrocarbons have been detected in several locations in soil samples and both surface and underground water.[33–35] Extensive measurements, including biomonitoring of dioxin levels in human tissues, are currently in progress.[36]

The association between the waste index and several health endpoints is difficult to interpret also in consideration of the potential ecological bias; on the other hand the index may capture a variety of pathways through which harmful exposures occur in the local population. If so, risks are likely to be underestimated because causal agents are only approximated, with a likely non-differential exposure misclassification. In addition the health outcomes selected for this study represent only a part of the possible health impacts: preliminary analyses indicate associations similar to those here described also with non-cancer mortality (data not shown). The adverse effect on non-cancer endpoints is not inconsistent with effects on cancer mortality, as living in an area with intensive uncontrolled waste disposal has visual, olfactory and safety implications which impinge on perceived health, quality of life and stress.

More research is needed, and more complete data on congenital anomalies are desirable, to confirm and describe the existence of multiple risks due to the complex mix of exposures associated with poorly managed and uncontrolled waste dumping and burning, to clarify which agents and which pathways are most important, to explore the effects with regard to more health outcomes and to evaluate the health impact of these exposures. It is, however, more urgent that action is undertaken in the region for removing the most acute cases of waste-related exposures and for implementing an efficient cycle of waste management. Insights from Campania may be valuable elsewhere: recent reports from international agencies indicate that waste mismanagement occurs in Europe and beyond, with substantial illegal shipment of hazardous waste, especially from the Organisation for Economic Co-operation and Development countries to new EU member states, Balkan countries and the Commonwealth of Independent States[37] and substantial quantities of waste dumped in illegal sites.[38] Illegal transport and disposal of hazardous waste is also a reason for concern in Africa, due to the economic profitability of uncontrolled dumping in countries where regulations are absent or not adequately enforced.[39]

### Main messages

- Urban, industrial and toxic waste has been illegally or inappropriately disposed for at least two decades in the provinces of Naples and Caserta, resulting in high environmental pressures and likely human exposure to a variety of agents, including toxic ones.
- Overall mortality, cancer mortality for several causes and congenital anomalies, previously known to be higher than regional averages, are positively correlated to waste exposure within the area, at small area level (municipality).
- While interpretation of the findings is difficult, due to approximate exposure data and other limitations in data quality and study design, their overall consistency suggests a possible role of waste-related exposures.

### Policy implications

These findings strengthen the case for urgent clean-up of contaminated areas, adoption of proper waste management practices, and eradication of illegal waste trafficking in the Campania region and in other European countries where illegal hazardous waste disposal occurs.

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## APPENDIX

**Table A1** Classification scheme for the 227 waste dumping sites included in the analysis. Sites were grouped into seven categories, from most hazardous (1) to least hazardous ones (7) by expert judgement

| Rank | Hazard | Type of sites |
|---|---|---|
| 1 | Possible presence of highly toxic and/or radioactive waste, impossible to investigate | Underwater wastes (in lakes) |
| 2 | Presence of hazardous waste | ► Scrap heaps of hazardous wastes<br>► Storing and treatment of toxic and hazardous wastes<br>► Abandonment of metallic drums (containers) |
| 3 | Limited presence of hazardous waste | Heaps in caves with presence of some hazardous waste |
| 4 | Presence of special waste of industrial origin with potential release of hazardous substances | Authorised landfill (II category, type B – special and industrial wastes) |
| 5 | Presence of non-hazardous waste with potential release of hazardous substances | ► Vehicle demolition/scrapping plants<br>► Plants for recovery of electrical and electronic wastes<br>► Sites of temporary storing of non-hazardous wastes<br>► Plants for physicochemical treatment of non-hazardous wastes<br>► Plants for recovery of non-hazardous wastes<br>► Plants for treatment (storing) of special wastes<br>► Plants for incineration of special wastes for oil regeneration |
| 6 | Presence of non-hazardous wastes in uncontrolled settings | ► Uncontrolled landfills of urban solid wastes<br>► Scrap heaps (>10 000 $m^3$) of non-hazardous wastes (in caves)<br>► Scrap heaps (>10 000 $m^3$) of non-hazardous wastes |
| 7 | Presence of non-hazardous wastes in controlled situations | ► Controlled landfills of urban solid wastes<br>► Controlled landfills of inert wastes<br>► Composting plant<br>► Plants for selection and production of refuse-derived fuel<br>► Plants for waste water treatment<br>► Scrap heaps of non-hazardous industrial wastes |