Environmental Exposures and Cancer

Morbidity and mortality of people who live close to municipal waste landfills: a multisite cohort study

Francesca Mataloni,1* Chiara Badaloni,1 Martina Nicole Golini,1 Andrea Bolignano,2 Simone Bucci,1 Roberto Sozzi,2 Francesco Forastiere,1 Marina Davoli1 and Carla Ancona1

1Department of Epidemiology, Lazio Regional Health Service, Rome, Italy and 2Lazio Environmental Protection Agency, Rome, Italy

*Corresponding author. Department of Epidemiology, Lazio Regional Health Service, Via Cristoforo Colombo, 112. 00147 Rome, Italy. E-mail: f.mataloni@deplazio.it

Accepted 27 January 2016

Abstract

Background: The evidence on the health effects related to residing close to landfills is controversial. Nine landfills for municipal waste have been operating in the Lazio region (Central Italy) for several decades. We evaluated the potential health effects associated with contamination from landfills using the estimated concentration of hydrogen sulphide (H2S) as exposure.

Methods: A cohort of residents within 5 km of landfills was enrolled (subjects resident on 1 January 1996 and those who subsequently moved into the areas until 2008) and followed for mortality and hospitalizations until 31 December 2012. Assessment of exposure to the landfill (H2S as a tracer) was performed for each subject at enrolment, using a Lagrangian dispersion model. Information on several confounders was available (gender, age, socioeconomic position, outdoor PM10 concentration, and distance from busy roads and industries). Cox regression analysis was performed [Hazard Ratios (HRs), 95% confidence intervals (CIs)].

Results: The cohort included 242 409 individuals. H2S exposure was associated with mortality from lung cancer and respiratory diseases (e.g. HR for increment of 1 ng/m3 H2S: 1.10, 95% CI 1.02–1.19; HR 1.09, 95% CI 1.00–1.19, respectively). There were also associations between H2S and hospitalization for respiratory diseases (HR = 1.02, 95% CI 1.00–1.03), especially acute respiratory infections among children (0–14 years) (HR = 1.06, 95% CI 1.02–1.11).

Conclusions: Exposure to H2S, a tracer of airborne contamination from landfills, was associated with lung cancer mortality as well as with mortality and morbidity for respiratory diseases. The link with respiratory disease is plausible and coherent with previous studies, whereas the association with lung cancer deserves confirmation.

Key words: waste, landfills, residential cohort study
Introduction

People who live close to municipal solid waste (MSW) landfills could be exposed to air pollutants emitted by the plants (landfill gas containing methane, carbon dioxide, hydrogen sulphide and other contaminants including volatile organic compounds, particulate matter and bioaerosols) or to contaminated soil and water. The possible health effects related to residence close to these sites have been assessed in several original papers1–9 and evaluated in systematic reviews.10,11 Excess of mortality for some cancer sites (e.g. liver, pancreas, kidney, larynx) and non-Hodgkin lymphoma has been noted in some studies,1–3 but the results have not been confirmed in other investigations.4–6 In addition, some studies have indicated an increase of respiratory symptoms among residents close to biodegradable waste facilities.12 In 2009, Porta et al.10 concluded that evidence of an association between living close to a landfill and adverse health effects is inconclusive. Most of the published studies have methodological problems, including poor exposure assessment based only on distance from the source, use of health data at the aggregate level and limited possibility of adjusting for socioeconomic status. The quality of the epidemiological studies and scientific knowledge about the issue would be improved by using a residential cohort approach13 and applying dispersion models to provide a better exposure assessment.14

This study aimed at evaluating the association between estimated exposure to hydrogen sulphide (H2S, produced by anaerobic decomposition of sulphur-containing organic matter in landfills) and mortality and morbidity of a cohort of residents living within 5 km of the nine MSW landfills of the Lazio region (Central Italy, about 5 million inhabitants including the city of Rome). The study was part of a larger project on the characteristics of municipal solid waste treatment plants, their emissions and potential health effects in Lazio (www.eraslazio.it).

Methods

Study areas

Nine municipal solid waste landfills have been operating in Lazio for several decades. Only in the past two decades they were equipped with containments (including leachate collection and treatment, landfill cap construction and landfill gas collection and treatment). The main characteristics of the landfills (together with other potentially relevant environmental factors in the areas, e.g. arsenic contamination)14 are described in Supplementary Table 1, Landfill characteristics, and in Supplementary Figure 2, Study areas, (available as Supplementary data at IJE online). The study area was defined for each landfill as a 5-km radius from the boundary of the landfills assessed using GIS software and regional technical maps with a scale of 1:5000. The World Geodetic System of 1984, with the Universal Transverse Mercator zone 33Nord projection (WGS84_UTM33N) was the reference for the geographical coordinates.

Exposure assessment

H2S has been considered a surrogate measure of all contaminants emitted by landfills, and the airborne concentrations were predicted using a dispersion model. Dispersion models, such as the one we have been using here, have been recently used to assess the health effects of waste management processes.15–17 We followed a process in three steps. First, yearly H2S emissions from each sector of the landfills were estimated using a Landfill Gas Emissions Model.18 Using several variables (the start and end dates of operations for each sector of the landfills, the waste capacity and waste acceptance rate), the annual emission rates for H2S were calculated by means of a first-order decomposition rate equation:

\[ Q_{H2S} = \sum_{t=1}^{n} \sum_{j=1}^{1} KL_0 \left( \frac{M_j}{10} \right) e^{-kt} \]

where:

- \( Q_{H2S} \) = annual emission rate (m³/year)
- \( t \) = age of the jth section of the landfill
- \( i \) = 1 year time increment
- \( n \) = (year of the calculation) – (initial year of waste acceptance)
\[ j = 0.1 \text{ year time increment} \]
\[ K = \text{hydrogen sulphide generation rate (year\textsuperscript{-1})} \]
\[ L_o = \text{potential hydrogen sulphide generation capacity (m}^3/\text{Mg}) \]
\[ M_t = \text{mass of waste accepted until } t \text{ (in Mg)} \]
\[ tij = \text{age of the waste mass accepted until the } i\text{th year (M_t) at the } j\text{th section} \]
\[ Mg = \text{Megagram.} \]

We used inventory defaults parameters derived from the US Environmental Protection Agency (EPA) Compilation of Air Pollutant Emission Factors\textsuperscript{19} to define hydrogen sulphide generation rate (K) and potential hydrogen sulphide generation capacity (L\textsubscript{o}), and Mt and tij were defined by the Lazio Environmental Protection Agency (EPA) using local data. Second, the EMMA software was used for the temporal and spatial modulation of the estimated emissions. EMMA approximates landfills shape as a regular grid with a resolution of 125 m x 125 m.\textsuperscript{20} Finally, we used a Lagrangian particle model (SPRAY ver.5, ARIANET Srl, Italy) to simulate H\textsubscript{2}S concentrations around the landfills and to produce maps of annual average concentrations around the sites; 2008 was chosen as the reference year for all the sites. The meteorological data were derived from regional measurements made by Lazio EPA in 2005 (that year is considered representative of the meteorological conditions in the area), and used in connection with RAMS data.\textsuperscript{21} The Lagrangian model simulates the transport, dispersion and deposition of pollutants emitted using the orography, the meteorological data, the turbulence and the hourly spatial distribution (horizontal and vertical) of the emissions, based on the characteristics of the single source and on the mass fluxes. The model follows the path of fictitious particles in the atmospheric turbulent flow, and it is able to take into account complex situations, such as the presence of obstacles, breeze cycles, strong meteorological non-homogeneities and non-stationary, calm wind conditions.

Each subject in the cohort (see below) was assigned an H\textsubscript{2}S exposure value corresponding to the estimated annual average value from the dispersion model at the baseline address. In other words, no exposure variation over time was considered and each person remained at the same exposure level during the all study period.

**Enrolment of the cohort and follow-up procedures**

All residents living within 5 km of the borders of the landfill on 1 January 1996, or those who later moved to the areas until 31 December 2008, were enrolled; datasets from 16 municipalities were used. Vital status was assessed using local registries until 31 December 2012. We considered subjects at risk until they died or moved out of the municipality.

**Health outcomes**

We analysed natural and cause-specific mortality and hospital admissions for cardiorespiratory diseases. The underlying cause of death for deceased subjects was retrieved from the Regional Registry of Causes of Death, and hospital admissions were obtained from the Regional Hospital Information System which collects information related to all hospital admissions that occur each year in public and private hospitals. Causes of death and diagnoses of hospitalization were coded according to the ICD 9 revision. For each subject, only the principal diagnosis that was the reason for the hospitalization was used and the event (i.e. failure in the Cox model) was defined at the time of the first hospitalization for a specific cause that occurred in the study period. Respiratory hospital admissions for children (residents under 14 years) were also analysed.

**Covariates**

We considered for each subject an area-based socioeconomic position (SEP) index, based on several characteristics at the census tract level (around 400 inhabitants) such as education level, occupation, housing conditions, family size and country of origin, classified into five levels (high, middle-high, medium, middle-low, low).\textsuperscript{22} Modelled outdoor PM\textsubscript{10} concentrations (µg/m\textsuperscript{3}) from primary emissions were assigned to the residential addresses of the cohort participants as a measure of background air quality.\textsuperscript{23} The dispersion model was based on the integration between the meteorological Regional Atmospheric Modelling System\textsuperscript{21} and the Eulerian Flexible Air Quality Regional Model (FARM, ARIANET Srl, Italy). As an additional indicator of long-term exposure to traffic-related air pollution at the baseline address, we used the Functional Road Class (FRC) (included in the TeleAtlasMultiNet road network) to classify the type of street: motorway (FRC = 0) and major traffic roads (FRC = 1–5). Presence of an industrial plant in the 2-km buffer from the residence was also considered. Information on individual lifestyle factors was not available.

**Statistical analysis**

The association between landfill H\textsubscript{2}S exposure and mortality and hospital admissions was evaluated using Cox proportional hazard regression models [hazard ratios (HRs), 95% confidence intervals (CIs)], with age as the underlying time variable.
For mortality we defined a latency period of 5 years; therefore we considered all cohort participants who were residents of the area on 1 January 1996 (and started the follow-up on 1 January 2001) and those who subsequently moved to the area up until 31 December 2003 (starting the follow-up 5 years after enrolment). No latency was allowed for the analyses of cardiorespiratory hospitalizations. We first compared the mortality and hospitalization risk of residents according to quartiles of the H$_2$S distribution. We then considered H$_2$S as a continuous variable, using the value of the annual mean exposure at residence. A linear association was estimated for increments equal to 1 ng/m$^3$ of H$_2$S. We considered as potential confounders socioeconomic position (SEP), PM$_{10}$ background concentrations, residence within 150 m of main roads, 500 m from high-traffic roads, and within 1 or 2 km of industrial plants. With the exception of PM$_{10}$, which was a continuous variable, all other covariates were considered in the model as categorical variables. In addition, the analyses were performed stratifying in the Cox analysis by landfill sites, to take into account the possible different background rates in the various local areas, by gender and by calendar period (1996–2000, 2001–04, 2005–08, 2009–12), to take into account possible time-related changes in background rates of mortality and hospitalization. Diagnostic tools were used to check the proportional-hazard assumption for all categorical covariates. If any variable in the individual cohort models violated this assumption, effect estimates were compared with a stratified Cox analysis for that covariate. SAS (SAS Institute, NC) and STATA ver. 12 (StataCorp, TX) software programs were used for the statistical analyses.

Results

A total of 242,409 individuals were enrolled in the cohort from 1996 to 2008 (50.4% females), and H$_2$S concentrations were estimated for each of them at the address of recruitment. The annual average H$_2$S exposure levels of the population was rather low, 6.3 ng/m$^3$ [standard deviation (SD) 22.5]; as expected, people living close to the largest landfills (Latina and Rome) had higher H$_2$S exposure levels [mean = 32.7 ng/m$^3$ (SD 76.3) and mean = 45.8 ng/m$^3$ (SD 59), respectively].

The main characteristics of the study cohort according to H$_2$S concentrations (divided by quartiles of exposure) are described in Table 1. The distribution of gender, age and vital status was rather similar across exposure categories. However, people living in areas with higher concentrations of H$_2$S were more likely to be of lower SEP compared with people living in areas with lower exposure. PM$_{10}$ background concentrations were higher in the most exposed group compared with those in the low exposure category. People in the higher exposure category tended to live farther from high traffic roads (500 m) but closer to highways and industrial plants (0–1 km). There was a good correlation between distance from landfill and H$_2$S exposure.

At the end of the follow-up there were 18,609 deaths (7.7%), and for 40,740 subjects (16.8%) the follow-up ended at the time of move away from the municipality of residence.

Table 2 shows the association between H$_2$S concentrations and cause-specific mortality; effect estimates are given for the quartile distribution of H$_2$S (25–50, 50–75, >75 percentile of the distribution vs <25 percentile) and for a linear increase of H$_2$S equal to 1 ng/m$^3$. There were associations between H$_2$S exposure and lung cancer (HR 1.34, 95% CI 1.06–1.71), and respiratory diseases (HR 1.30, 95% CI 0.99–1.70) when comparing residents in areas with H$_2$S concentrations greater than 75 percentiles to the reference group. These findings were confirmed when we consider H$_2$S exposure as linear (HR 1.10, 95% CI 1.02–1.19 for lung cancer and HR 1.09, 95% CI 1.00–1.19 for respiratory diseases). No other associations were noted.

Table 3 shows the results for cardiorespiratory hospital admissions. No association was detected for cardiovascular diseases. There was an association between the highest quartile of exposure to H$_2$S and hospitalizations for respiratory diseases (HR 1.05, 95% CI 0.99–1.11) also when considering H$_2$S exposure as a linear term in the model. We found an association with paediatric admissions for asthma but with wider confidence intervals. In both mortality and hospitalization analyses, we did not find effect modification by gender (data not shown).

Because of the peculiarity of the urban site in Rome (‘Malagrotta’) (where a large landfill, an incinerator of medical wastes, and a petrochemical refinery are located within just a few kilometres of each other$^3$), we repeated the analyses excluding the subjects who live close to the Malagrotta landfill. There were no important changes in the results (See Supplementary Tables 3 ‘Mortality excluding Malagrotta landfill’ and 4 ‘Morbidity excluding Malagrotta landfill’, available as Supplementary data at IJE online). We did perform the same sensitivity analysis excluding each landfill at the time, and again the results were similar (see Supplementary Figures 7 ‘Lung cancer mortality’, 8 ‘Respiratory mortality’, 9 ‘Respiratory morbidity’ and 10 ‘Respiratory morbidity in children’, available as Supplementary data at IJE online).
An additional analysis was performed using distance from the landfills (0–2 km, 2–3 km vs 3–5 km), instead of estimated H₂S concentration, as the exposure variable. Although the results for mortality using distance were not similar to what has been observed using H₂S concentrations (see Supplementary Table 5 ‘Mortality by distance’, available as Supplementary data at *IJE* online) the results for hospitalizations were similar to those obtained using H₂S concentrations (see Supplementary Table 6 ‘Morbidity by distance’, available as Supplementary data at *IJE* online).

Our final concern was that migration outside the areas could bias the results in the case of migration being associated with the exposure and if residents with pre-existing diseases were more likely to migrate. We compared the characteristics of people who migrated outside the study.

### Table 1. Descriptive individual and environmental characteristics of the cohort members by hydrogen sulphide (H₂S) exposure

| Total | H₂S exposure levels (ng/m³) |
|-------|-----------------------------|
|       | <2.5° perc (<0.77) | 2.5°–5.0° perc (0.77–2.1) | 5.0°–7.5° perc (2.1–4.2) | >7.5° perc (>4.2) |
| No. % | No. % | No. % | No. % |
|-------|-------|-------|-------|
| Total | 242,409 | 100 | 60,927 | 100.0 | 60,775 | 100 | 63,962 | 100 | 56,745 | 100 |
| Gender | | | | | | | | | | |
| Males | 120,232 | 49.6 | 29,781 | 49.0 | 30,137 | 49.6 | 31,979 | 50.0 | 28,335 | 49.9 |
| Females | 122,177 | 50.4 | 31,146 | 51.0 | 30,638 | 50.4 | 31,983 | 50.0 | 28,410 | 50.1 |
| Vital status | | | | | | | | | | |
| Alive | 183,060 | 75.5 | 48,306 | 79.3 | 45,948 | 75.6 | 44,673 | 69.8 | 44,133 | 77.8 |
| Migrant | 40,740 | 16.8 | 10,228 | 16.8 | 14,446 | 22.6 | 7,897 | 13.9 |
| Dead | 18,609 | 7.7 | 4,599 | 7.6 | 4,843 | 7.6 | 4,715 | 8.3 |
| Age at recruitment (years) | | | | | | | | | | |
| 0–14 | 53,082 | 21.9 | 12,246 | 20.0 | 13,011 | 21.4 | 16,266 | 25.4 | 11,559 | 20.4 |
| 15–44 | 112,754 | 46.5 | 27,380 | 45.0 | 28,383 | 46.7 | 30,661 | 47.9 | 26,330 | 46.4 |
| 45–64 | 50,146 | 20.7 | 13,296 | 22.0 | 12,584 | 20.7 | 11,727 | 18.3 | 12,539 | 22.1 |
| >65 | 26,427 | 10.9 | 6,995 | 11.2 | 5,308 | 8.3 | 6,317 | 11.1 |
| Area-based socioeconomic position | | | | | | | | | | |
| High | 23,589 | 9.7 | 10,012 | 16.0 | 6,033 | 9.9 | 4,779 | 7.5 | 2,765 | 4.9 |
| Middle-high | 41,955 | 17.3 | 7,843 | 12.0 | 8,834 | 14.5 | 9,548 | 14.9 | 15,730 | 27.7 |
| Medium | 42,286 | 17.4 | 7,447 | 12.0 | 8,588 | 14.1 | 13,958 | 21.8 | 12,293 | 21.7 |
| Middle-low | 50,394 | 20.8 | 5,364 | 9.0 | 16,816 | 27.7 | 17,563 | 27.5 | 10,651 | 18.8 |
| Low | 62,157 | 25.6 | 22,806 | 37.0 | 15,206 | 25.0 | 11,906 | 18.6 | 12,239 | 21.6 |
| Missing | 22,028 | 9.1 | 7,455 | 12.0 | 5,298 | 8.7 | 6,208 | 9.7 | 3,067 | 5.4 |
| PM₁₀ (µg/m³) | | | | | | | | | | |
| < 11.99 (<50° perc) | 121,222 | 50.0 | 44,371 | 73.0 | 29,696 | 48.9 | 23,986 | 37.5 | 23,169 | 40.8 |
| 11.99–17.69 (50°–90° perc) | 96,369 | 39.8 | 16,556 | 27.0 | 28,967 | 47.7 | 31,661 | 49.5 | 19,185 | 33.8 |
| > 17.69 (>90° perc) | 24,818 | 10.2 | 0.0 | 0.0 | 2,112 | 3.5 | 8,315 | 13.0 | 14,391 | 25.4 |
| Distance from major roads (metres) | | | | | | | | | | |
| < = 150 m | 114,698 | 47.3 | 31,842 | 52.0 | 25,876 | 42.6 | 34,506 | 53.9 | 22,474 | 39.6 |
| > 150 m | 127,711 | 52.7 | 29,085 | 48.0 | 34,899 | 57.4 | 29,456 | 46.1 | 34,271 | 60.4 |
| Distance from highways (metres) | | | | | | | | | | |
| < = 500 m | 9,428 | 3.9 | 2,908 | 5.0 | 1,087 | 1.8 | 744 | 1.2 | 4,689 | 8.3 |
| > 500 m | 232,981 | 96.1 | 58,019 | 95.0 | 59,688 | 98.2 | 63,218 | 98.8 | 52,056 | 91.7 |
| Distance from industrial plants (km) | | | | | | | | | | |
| 0–1 km | 12,863 | 5.3 | 376 | 1.0 | 2,676 | 4.4 | 1,130 | 1.8 | 8,681 | 15.3 |
| 1–2 km | 50,503 | 20.8 | 1,138 | 2.0 | 9,589 | 15.8 | 28,809 | 45.0 | 10,967 | 19.3 |
| > 2 km | 179,043 | 73.9 | 59,413 | 98.0 | 48,510 | 79.8 | 34,023 | 53.2 | 37,097 | 65.4 |
| Distance from landfill (km) | | | | | | | | | | |
| 0–1 km | 5,187 | 2.1 | 0.0 | 0.0 | 3 | 0.0 | 19 | 0.0 | 5,165 | 9.1 |
| 1–2 km | 21,475 | 8.9 | 2.0 | 0.0 | 4,225 | 7.0 | 5,835 | 9.1 | 11,413 | 20.1 |
| 2–3 km | 65,386 | 27.0 | 8,372 | 13.7 | 20,588 | 33.9 | 23,627 | 36.9 | 12,799 | 22.6 |
| 3–4 km | 77,722 | 32.1 | 19,739 | 32.4 | 18,878 | 30.9 | 20,217 | 31.6 | 18,979 | 33.4 |
| 4–5 km | 72,639 | 30.0 | 32,814 | 53.9 | 17,172 | 28.3 | 14,264 | 22.3 | 8,389 | 14.8 |
| Cause of death (ICD-9-CM) | \( \text{H}_2\text{S} \) concentrations | No. | Crude HR | HR | 95% CI | No. | Crude HR | HR | 95% CI | No. | Crude HR | HR | 95% CI | HR | 95% CI |
|--------------------------|--------------------------------------|-----|---------|-----|--------|-----|---------|-----|--------|-----|---------|-----|--------|-----|--------|
| Natural causes (001–799) | \(<25^{\text{th}}\) percentile\(^a\) | 3701 | 3946 | 0.98 | 1.01 (0.96–1.06) | 4254 | 1.00 | 1.02 (0.97–1.08) | 4104 | 0.96 | 0.98 (0.91–1.05) | 1.00 (0.98–1.02) |
| All cancers (140–239)   | \(25^{\text{th}}–50^{\text{th}}\) percentile | 1282 | 1307 | 0.97 | 0.99 (0.91–1.08) | 1493 | 1.03 | 1.05 (0.95–1.16) | 1452 | 1.00 | 1.03 (0.91–1.16) | 1.01 (0.98–1.05) |
| Stomach (151)           | \(50^{\text{th}}–75^{\text{th}}\) percentile | 75 | 88 | 1.03 | 0.98 (0.70–1.37) | 108 | 1.27 | 1.23 (0.84–1.79) | 105 | 1.00 | 0.88 (0.54–1.42) | 1.00 (0.87–1.16) |
| Colorectal (153–154,159) | \(>75^{\text{th}}\) percentile | 154 | 170 | 0.99 | 1.00 (0.79–1.27) | 176 | 0.96 | 0.97 (0.74–1.28) | 159 | 0.93 | 0.91 (0.64–1.28) | 0.97 (0.87–1.08) |
| Liver (155–156)         | \(\text{Linear trend}\) | 102 | 89 | 0.86 | 0.83 (0.61–1.13) | 106 | 0.89 | 0.77 (0.53–1.11) | 107 | 0.74 | 0.76 (0.48–1.2) | 0.90 (0.78–1.05) |
| Pancreas (157)          | \(\text{Reference category}\) | 68 | 64 | 0.92 | 0.93 (0.64–1.35) | 69 | 0.92 | 0.95 (0.61–1.49) | 72 | 0.69 | 0.73 (0.41–1.32) | 0.93 (0.77–1.11) |
| Larynx (161)            | \(1.00–1.10\) | 17 | 15 | 0.81 | 0.72 (0.33–1.56) | 11 | 0.38 | 0.40 (0.14–1.14) | 23 | 0.43 | 0.26 (0.07–0.95) | 0.64 (0.43–0.97) |
| Lung (162)               | \(1.10–1.20\) | 276 | 281 | 0.98 | 1.06 (0.89–1.27) | 360 | 1.09 | 1.18 (0.97–1.45) | 361 | 1.19 | 1.34 (1.06–1.71) | 1.10 (1.02–1.19) |
| Bladder (188)           | \(1.20–1.30\) | 54 | 48 | 0.88 | 0.89 (0.59–1.36) | 56 | 1.22 | 1.33 (0.81–2.16) | 50 | 1.01 | 0.94 (0.5–1.80) | 1.03 (0.85–1.26) |
| Kidney (189)            | \(1.30–1.40\) | 36 | 30 | 0.76 | 0.85 (0.51–1.43) | 36 | 0.87 | 0.94 (0.52–1.70) | 31 | 0.70 | 0.86 (0.41–1.83) | 0.96 (0.75–1.22) |
| Brain (191)             | \(1.40–1.50\) | 23 | 29 | 1.26 | 1.25 (0.70–2.26) | 38 | 1.63 | 1.63 (0.84–3.17) | 41 | 1.70 | 1.76 (0.81–3.81) | 1.22 (0.95–1.56) |
| Lymphatic and haematopoietic tissue (200–208) | \(1.50–1.60\) | 108 | 115 | 1.03 | 1.16 (0.87–1.54) | 106 | 0.94 | 0.96 (0.66–1.35) | 102 | 1.06 | 1.12 (0.74–1.77) | 1.02 (0.89–1.16) |
| Cardiovascular diseases (390–459) | \(1.70–1.80\) | 1457 | 1681 | 1.02 | 1.05 (0.97–1.13) | 1676 | 0.96 | 1.00 (0.91–1.09) | 1641 | 0.90 | 0.91 (0.81–1.02) | 0.98 (0.94–1.01) |
| Ischaemic heart diseases (410–414) | \(1.20–1.30\) | 512 | 570 | 0.99 | 1.00 (0.88–1.14) | 574 | 0.86 | 0.91 (0.78–1.06) | 530 | 0.77 | 0.78 (0.64–0.95) | 0.93 (0.87–0.99) |
| Respiratory diseases (460–519) | \(1.40–1.50\) | 256 | 244 | 0.88 | 0.92 (0.76–1.11) | 279 | 1.15 | 1.13 (0.90–1.40) | 264 | 1.30 | 1.30 (0.99–1.70) | 1.09 (1.00–1.19) |
| Digestive diseases (520–579) | \(1.50–1.60\) | 158 | 163 | 0.93 | 0.97 (0.77–1.24) | 218 | 1.06 | 1.09 (0.83–1.41) | 186 | 0.94 | 0.97 (0.69–1.35) | 1.01 (0.91–1.12) |
| Urinary system diseases (580–599) | \(1.70–1.80\) | 58 | 92 | 1.49 | 1.54 (1.08–2.21) | 74 | 1.25 | 1.28 (0.83–1.97) | 67 | 1.26 | 1.42 (0.84–2.40) | 1.11 (0.94–1.30) |

\(^a\)Reference category
areas (40,740 subjects) with those who remained in the areas until the end of the follow-up (201,669 subjects). See Supplementary Table 11 ‘Comparison between migrant and not migrant’, available as Supplementary data at IJE online. We considered gender, age, socioeconomic status and H2S exposure as fixed variables. Since occurrence of hospitalizations before migration is a time-dependent variable, we compared subjects migrating in the period 2004–12 (19,695 subjects) with all subjects who did not migrate before that period (189,560 subjects), evaluating the occurrence of cardiorespiratory hospitalizations during 1998–2003. Migration was associated with male gender, younger age and lower exposure to H2S; no clear differences of migrants compared with non-migrants were found for socioeconomic status. In a multinomial logistic regression (data not shown), we found no major differences between the two groups for respiratory diseases, whereas migrants were less likely than non-migrants to suffer from two or more hospitalizations for cardiovascular disease (OR, 0.74; 95% CI 0.57–0.95) before migrating. All these results indicate that bias due to increased susceptibility of migrants is unlikely given that migrants are less exposed and tend to be healthier than non-migrants.

Discussion

We found a positive association between exposure to hydrogen sulphide (H2S), that we used as a surrogate for all the pollutants co-emitted from the landfills, and mortality for lung cancer and respiratory diseases as well as hospitalizations for respiratory diseases, especially in children.

Table 3. Associations between hydrogen sulphide (H2S, in quartiles and continuous) and cardiorespiratory morbidity: number of people hospitalized (No.), hazard ratios (HR) and 95% confidence intervals (95% CI)

| Diagnosis (ICD-9-CM) | H2S concentrations* | 25<–75 percentile | 75<–25 percentile | Linear trend |
|----------------------|---------------------|------------------|------------------|-------------|
|                      |                     | No. | Crude HR | HR 95% CI | No. | Crude HR | HR 95% CI | No. | Crude HR | HR 95% CI |
| Total cohort         |                     |     |          |           |     |          |           |     |          |           |
| Cardiovascular diseases (390–459) | 6 666 | 6 090 | 0.99 | (0.95–1.03) | 6 291 | 0.99 | 1.00 | (0.96–1.04) | 6 677 | 1.03 | 1.02 | (0.97–1.07) | 1.00 | (0.99–1.02) |
| Cardiac diseases (390–429) | 3 991 | 3 585 | 0.99 | (0.93–1.03) | 3 580 | 0.97 | 1.00 | (0.92–1.04) | 4 022 | 1.05 | 1.04 | (0.97–1.11) | 1.01 | (0.98–1.03) |
| Ischaemic heart diseases (410–414) | 1 393 | 1 347 | 1.03 | (1.01–1.07) | 1 288 | 0.94 | 1.04 | (0.85–1.03) | 1 426 | 1.01 | 0.99 | (0.88–1.10) | 0.99 | (0.95–1.02) |
| Cerebrovascular diseases (430–438) | 1 635 | 1 482 | 0.98 | (0.91–1.06) | 1 466 | 0.97 | 0.97 | (0.89–1.06) | 1 543 | 0.97 | 0.98 | (0.88–1.10) | 0.99 | (0.96–1.03) |
| Respiratory diseases (460–519) | 4 372 | 4 249 | 0.98 | (0.92–1.01) | 5 628 | 1.02 | 1.01 | (0.96–1.06) | 4 837 | 1.06 | 1.05 | (0.99–1.11) | 1.02 | (1.00–1.03) |
| Acute respiratory infections (460–464,480–487) | 1 447 | 1 441 | 1.00 | (0.89–1.04) | 1 721 | 1.00 | 0.97 | (0.89–1.05) | 1 509 | 1.09 | 1.07 | (0.97–1.18) | 1.02 | (0.98–1.05) |
| COPD (490–492,494,496) | 674 | 592 | 0.96 | (0.84–1.06) | 535 | 0.92 | 0.90 | (0.78–1.04) | 377 | 1.09 | 1.06 | (0.90–1.25) | 1.00 | (0.95–1.03) |
| Asthma (493) | 332 | 355 | 1.01 | (0.86–1.17) | 394 | 1.16 | 1.17 | (0.99–1.18) | 365 | 1.11 | 1.09 | (0.90–1.33) | 1.04 | (0.98–1.11) |
| Children 0–14 years old |                     |     |          |           |     |          |           |     |          |           |
| Respiratory diseases (460–519) | 1 447 | 1 522 | 1.00 | (0.92–1.07) | 2 420 | 1.07 | 1.08 | (0.99–1.17) | 1 499 | 1.10 | 1.11 | (1.01–1.22) | 1.04 | (1.01–1.07) |
| Acute respiratory infections (460–464,480–487) | 573 | 669 | 1.10 | (0.91–1.15) | 925 | 1.15 | 1.10 | (0.97–1.25) | 617 | 1.25 | 1.20 | (1.04–1.38) | 1.06 | (1.02–1.11) |
| Asthma (493) | 247 | 267 | 0.98 | (0.83–1.19) | 506 | 1.23 | 1.29 | (1.06–1.55) | 276 | 1.11 | 1.13 | (0.91–1.41) | 1.07 | (0.99–1.14) |

*Reference category
those who lived more than 2 km away.4 Despite the large statistical power, the study did not show excess cancer risk associated with proximity to landfill sites. An ecological study compared mortality, hospital admissions and reproductive health of a population living near a landfill site in Wales with another population matched for socioeconomic status.5 No differences between the two populations were found. A study in Brazil evaluated the association between residence close to solid waste landfill sites and cancer mortality.6 The exposed areas were defined using a 2-km buffer radius around 15 sites. Standardized mortality ratios were analysed in Bayesian spatial models. The results did not indicate any excess risk for people close to landfills. Some elevated risks of bladder and liver cancer, and death due to congenital malformation were found, although they did not have statistical significance.

The results we found regarding respiratory diseases are consistent with others suggesting a relationship between living close to landfill areas and damage to the respiratory system,24,25 as highlighted in a recent systematic review.26 Occurrence of respiratory symptoms was documented among residents living close to waste sites12 and was linked to inhalation exposure to endotoxin, microorganisms, and aerosols from waste collection and land filling.27

Occupational exposure to organic dust, particulate matters from microbial, plant or animal origin, has been associated with an increased risk of lung cancer in a pooled analysis of case-control studies.25 High lung cancer mortality was found among male residents of Italian National Priority Contaminated Sites with industrial waste landfills or illegal dumps29 and among residents living near incinerators and landfills of hazardous waste in Spain,30 but the overall evidence that residing near landfills is associated with increased risk of lung cancer is still inadequate.10

This study attempted to overcome some of the limitations of the previously conducted studies, which included issues of study design, exposure assessment and confounding.11 We used a residential cohort approach to provide a more detailed estimation of the population at risk. To each subject in the cohort we assigned an H2S exposure value (corresponding to the estimated H2S concentration at the baseline address). It was not possible to consider indexes of average or cumulative exposure based on the different residences, because only a few municipality databases provided information about changes of residence during the follow-up. For this reason, individual exposure reflects residence at the beginning of the follow-up.

Previous studies have considered distance from landfills as a proxy of exposure.4,7,8 Distance-to-source is easy to understand because it assumes that people living near the landfill are more exposed than people living further away. We used modelled H2S concentrations as an exposure measure of the landfill gases, on the assumption that the pollution from landfills does not spread uniformly around the site but depends on the quantity of incoming waste, the prevailing winds and the orography of the area.3 Our results for hospitalizations were confirmed when we used distance from the source as the exposure variable instead of modelled H2S concentrations. There are, however, several aspects in the exposure assessment process we used that should be considered. H2S generation rates were taken from EPA published material, and waste acceptance capacity and waste acceptance rates were from derived from legal authorized values. It is likely, then, that the derived absolute emissions data were more accurate for the recent period and less certain for the past. On the other hand, we used the shape of the H2S concentrations on the ground to rank subjects as more exposed or less exposed, and this shape is of greater importance than the exact absolute values. Of course, the major limitation of our exposure assessment is related to the lack of a validation study with in situ measurements. Nonetheless, SPRAY is a consolidated model that has been validated using a ‘conventional’ validation framework,31 and its performances and efficiency have been evaluated and validated in multiple real conditions with different orography, size of domain, number of grid cells in the domain, meteorological conditions and emission types.32–34 The model has been already used in other locations to study health effects of waste management.1,17 Another aspect of concern is the use of meteorological parameters that greatly influence the dispersion of the pollutants. We considered the year 2005 as representative of the study area meteorological conditions because there were no particular meteorological anomalies in that year. Running the dispersion model with meteorological data for different years could change the landfills footprint only in presence of extreme weather conditions that strongly affect the annual average. In our opinion, the difference among years is generally minimal and the uncertainty associated with the use of specific meteorological data is negligible.

Our results were adjusted for several confounders: age, socioeconomic position and variables related to the environmental context (proximity to roads with heavy traffic, proximity to industrial sites, air quality) that might otherwise distort the study association. In particular, high level of PM10 (> 90 percentile of the distribution vs < 50 percentile) was associated in our model with cardiovascular and respiratory hospitalizations (HR 1.08, 95% CI 1.01–1.16 and HR 1.03, 95% CI 0.96–1.12, respectively). However, no data were available on the personal habits of the subjects, which could have had a role in the diseases investigated, especially cigarette smoking but also alcohol use, physical activity and obesity. The collection of this
information, through telephone interviews or home visits, would have been prohibitive for such a large cohort, and the lack of this information may have biased the results because of confounding not controlled in the analysis. It should be noted, however, that many personal habits are associated with socioeconomic position. It is therefore reasonable to assume that the analysis that adjusted for socioeconomic index also took into account others individual variables, including smoking. Moreover, excess of hospitalizations for respiratory diseases were found also in children, and no excess mortality/morbidity for cardiovascular diseases (indicative of most of the unmeasured lifestyle factors including smoking) was found, despite the larger statistical power than for respiratory diseases. Therefore, although residual confounding cannot be excluded, it is unlikely that the observed relationship between H2S exposure and respiratory disturbances could be entirely due to unmeasured smoking habits and other factors.

In conclusion, we found associations between H2S exposure from landfills and mortality from lung cancer as well as mortality and morbidity for respiratory diseases. The link with respiratory diseases has been observed in other studies and it is potentially related to irritant gases and other organic contaminants. The excess of lung cancer is a relatively new finding.

Supplementary Data
Supplementary data are available at IJE online.

Funding
This study was supported by the Lazio Waste General Directorate (DGR n929/08) as a part of a larger project on the health effects of waste treatment plants in the Lazio region (ERAS Lazio: Epidemiology, Waste, Environment and Health —www.eraslazio.it). The funder had no scientific role.

Acknowledgements
We wish to thank Margaret Becker for her help in editing the manuscript and Carlo A. Perucci, former director of our department, for initiating the ERAS Lazio project and for his long-standing support of environmental epidemiology.

Conflict of interest: None declared.

References
1. Goldberg MS, Siemiatyck J, DeWar R, Dèsy M, Riberyd H. Risk of developing cancer relative to living near a municipal solid waste landfill site in Montreal, Quebec, Canada. Arch Environ Health 1999;54:291–96.
2. Michelozzi P, Fusco D, Forastiere F et al. Small area study of mortality among people living near multiple sources of air pollution. Occup Environ Med 1998;55:611–15.
3. Ancona C, Badaloni C, Mataloni F et al. Mortality and morbidity in a population exposed to multiple sources of air pollution: a retrospective cohort study using air dispersion models. Environ Res 2015;137:467–74.
4. Jarup L, Briggs D, de Hoogh C et al. Cancer risks in populations living near landfill sites in Great Britain. Br J Cancer 2002;86:1732–36.
5. Fielder HMP, Poon-King CM, Palmer S R et al. Assessment of impact on health of residents living near the Nant-y-Gwyydon landfill site: retrospective analysis. BMJ 2000;320:19–22.
6. Gouveia N, Prado RR. Health risks in areas close to urban solid waste landfill sites. Rev Saúde Publica 2010;44:859–66.
7. Pukkala E, Ponkä A. Increased incidence of cancer and asthma in houses built on a former dump area. Environ Health Perspect 2001;109:1121–25.
8. Forastiere F, Badaloni C, de Hoogh K et al. Health impact assessment of waste management facilities in three European countries. Environ Health 2011;10:53.
9. WHO. Population health and waste management: scientific data and available options. http://www.euro.who.int/document/E91021.pdf (24 March 2015, date last accessed).
10. Porta D, Milani S, Lazzarino AI et al. Systematic review of epidemiological studies on health effects associated with management of solid waste. Environ Health 2009;23:8–60.
11. Giusti L. A review of waste management practices and their impact on human health. Waste Manag 2009;29:2227–39.
12. Blanes-Vidal V, Baëlum J, Schwartz J et al. Respiratory and sensory irritation symptoms among residents exposed to low-to-moderate air pollution from biodegradable wastes. J Expo Sci Environ Epidemiol 2014;24:388–97.
13. Ancona C, Mataloni F, Badaloni C et al. Residential cohort approach in industrial contaminated sites: the ERAS Lazio project. Epidemiol Prev 2014;38(Suppl 1):158–61.
14. D’Ippoliti D, Santelli E, De Sario M et al. Arsenic in drinking water and mortality for cancer and chronic diseases in Central Italy, 1990-2010. PloS One 2015;10:e0138182.
15. Ranzi A, Fano V, Ersparmer L et al. Mortality and morbidity among people living close to incinerators: a cohort study based on dispersion modeling for exposure assessment. Environ Health 2011;10:22.
16. Candela S, Ranzi A, Bonvicini L et al. Air pollution from incinerators and reproductive outcomes: a multisite study. Epidemiology 2013;24:863–70.
17. Golini MN, Ancona C, Badaloni CA et al. Morbidity in a population living close to urban waste incinerator plants in Lazio Region (Central Italy): a retrospective cohort study using a before-after design. Epidemiol Prev 2014;38:323–34.
18. Alexander A, Burklin C, Singleton A et al. Landfill Gas Emissions Model (LandGEM) Version 3.02 User’s Guide, May 2005.
19. US Environmental Protection Agency. Compilation of Air Pollutant Emission Factors; AP-42. http://www3.epa.gov/ttnchie1/ap42/ (24 March 2015, date last accessed).
20. Calori G, Radice P. Emission Manager – Reference Guide. Milan, Italy: ARIANET R2004.29, 2004.
21. Pielke RA, Cotton WR, Wallko RL et al. A comprehensive Meteorological Modeling System RAMS. Meteorol. Atmos. Phys. 1992;49:69–91.
22. Cesaroni G, Agabiti N, Rosati R, Forastiere F, Perucci CA. An index of socioeconomic position based on 2001 Census, Rome. Epidemiol Prev 2006;30:352–57.
23. Sozzi R, Bolognano A, Barberini S, Di Giosa AD. Apporto sullo stato della qualità dell’aria nella Regione Lazio 2011. ARPA Lazio. 2012.
24. Heaney CD, Wing S, Campbell RL et al. Relation between malodor, ambient hydrogen sulfide, and health in a community bordering a landfill. Environ Res 2011;111:847–52.
25. Corrêa CR, Abrahão CE, Carpintero Mdo C, Anaruma Filho F. Landfills as risk factors for respiratory disease in children. J Pediatr (Rio J) 2011;87:319–24.
26. Mattiello A, Chiodini P, Bianco E et al. Health effects associated with the disposal of solid waste in landfills and incinerators in populations living in surrounding areas: a systematic review. Int J Public Health 2013;58:725–35.
27. Park DU, Ryu SH, Kim SB, Yoon CS. An assessment of dust, endotoxin, and microorganism exposure during waste collection and sorting. J Air Waste Manag Assoc 2011;61:461–68.
28. Peters S, Kromhout H, Olsson AC et al. Occupational exposure to organic dust increases lung cancer risk in the general population. Thorax 2012;67:111–16.
29. Fazzo L, Minichilli F, Pirastu R et al. A meta-analysis of mortality data in Italian contaminated sites with industrial waste landfills or illegal dumps. Ann Ist Super Sanità 2014;50:278–85.
30. García-Pérez J, Fernández-Navarro P, Castelló A et al. Cancer mortality in towns in the vicinity of incinerators and installations for the recovery or disposal of hazardous waste. Environ Int 2013;51:31–44.
31. Olesen HR. Toward the establishment of a common framework for model evaluation. In: Gryning SE, Schiermeier F (eds). Air Pollution Modeling and Its Application XI. New York, NY: Plenum Press, 1996.
32. Brusasca G, Tinarelli G, Anfossi D. Particle model simulation of diffusion in low windspeed stable conditions. Atmos Environ 1989;26, 707–723.
33. Brusasca G, Tinarelli G, Anfossi D. Comparison between the results of a Monte Carlo atmospheric diffusion model and tracer experiments, Atmosp Environ 1992;26:1263–80.
34. Anfossi D, Tinarelli G, TriniCastelli S et al. A new Lagrangian particle model for the simulation of dense gas dispersion. Atmos Environ 2010;44:753–62.