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ORIGINAL ARTICLE

Investigating mortality heterogeneity among neighbourhoods of a highly industrialised Italian city: a meta-regression approach

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Abstract

Objectives The purpose of this study was to investigate the role of various predictors to explain spatial mortality heterogeneity in Taranto.

Methods Direct age-adjusted death rates (ADR) at a neighbourhood level for the period 1998–2010 were examined. SO_2, PM_{10}, distance from pollution sources, and socioeconomic status (SES) were tested as predictors within a meta-regression framework. We used τ^2 to quantify heterogeneity in ADR and I^2 statistic with 95 % confidence intervals to estimate the proportion of total variation across neighbourhoods attributable to the between-neighbourhood heterogeneity.

Results High heterogeneity resulted for all and natural causes of death for both genders. One neighbourhood (Paolo VI) was detected as an outlier for all predictors except SO_2, among males. After accounting for SES, moderate heterogeneity among residuals was observed for all-causes of death and was correlated with SO_2. Higher concentrations of PM_{10} were observed in neighbourhoods close to the industrial site and higher concentrations of SO_2 in neighbourhoods more distant from the industrial site.

Conclusions SES and air pollutants were predictors of spatial heterogeneity in ADR. Different distributions of SO_2 and PM_{10} in the city suggested two exposure patterns.

Keywords Mortality differences · Taranto · Meta-analysis · Air pollution · Socioeconomic status

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Introduction

Highly industrialised areas often show spatial heterogeneity in health outcomes due to environmental pollution and socioeconomic status (SES). Indeed, health outcomes tend to be worse in areas characterised by high socioeconomic deprivation (Benach et al. 2001; Carstairs 2000; Davey Smith et al. 1998; Pickett and Pearl 2001; Thomas et al.

2010) and living near industrial facilities (Franchini et al. 2004; Loyo-Berrios et al. 2007) has long been known to represent a risk factor for human health due to high exposure to pollutants (Benedetti et al. 2001; Knox 2005). Moreover, one of the most important risk factors is air pollution, whose health effects have been intensely studied since the 1970s. Exposure to pollutants, such as nitrogen dioxide (NO_2), sulphur dioxide (SO_2), ozone (O_3), and particulate matter (PM) has been associated with increased mortality and hospital admissions due to respiratory and cardiovascular diseases (Andersen et al. 2010; Cesaroni et al. 2014; Hoek et al. 2013).

Taranto, a city in south-eastern Italy, suffers from environmental pollution and from substantial differences in the SES between neighbourhoods. Pollution derives from several industrial sources: one of the largest steel plants in Europe with more than 300 emitting stacks and large mineral deposit, oil refining, cement production, fuel storage, power production, waste materials management and mining as well as military installations. In 2011, the Court of Taranto ordered an epidemiological study to investigate the impact of the steel plant on population health. A cohort study (Forastiere et al. 2012) found various health problems critically associated with exposure to PM_{10} (particulate matter with a diameter 10 micrometres or less) and with SES (Mataloni et al. 2012), with an increased risk of morbidity and mortality among residents in neighbourhoods close to the industrial area. More recently, increased mortality rates compared to regional averages were found among neighbourhoods further away from the industrial areas (Vigotti et al. 2014). However, morbidity and mortality rates showed some heterogeneity between neighbourhoods. Indeed, higher rates were observed both among residents in Tamburi and Borgo (two neighbourhoods close to the steel plant) as well as in Paolo VI, a neighbourhood 5.6 km away from the plant (Forastiere et al. 2012) (Fig. 1).

In a recent study, Mangia and colleagues (Mangia et al. 2013) investigated the variability of criteria air pollutants (SO_2, PM_{10}, NO_2) in the city of Taranto. Their analysis revealed that: (1) the effects on the city of the various emission sources depend upon meteorological conditions; (2) the influence of the industrial site can be primarily identified with the SO_2 data, whereas the impact of the mineral deposit and other fugitive emissions can be shown through PM_{10} data. Previous work (Gariazzo et al. 2007) found analogous results, by applying a chemical transport model in several case studies. In fact, industrial activities were found to be the main contributor to the estimated ground concentrations of SO_2 and PM_{10} with the industry-derived SO_2 and PM_{10} values showing some variability within the city, with contributions to ambient SO_2 ranging from 70 to 97 % and contributions to ambient PM_{10} from 58 to 82 %.

Given this enormous heterogeneity in mortality between neighbourhoods and the suggestion that this might be due to nonuniform spatial distribution of social and environmental factors within the city, our aim is to study the relevance of such potential predictors of mortality in the highly industrialised city of Taranto.

Methods

Our study is based on direct age-adjusted death rates per 100,000 inhabitants (ADR), for the period 1998–2010 using the 1991 Italian population census as reference. ADR were taken from the cohort study ordered by the Court of Taranto (Forastiere et al. 2012) and published by Mataloni and colleagues as supplementary material (Mataloni et al. 2012). ADRs were computed separately for males and females at the neighbourhood level.

The following causes of death were chosen a priori for their high prevalence: all-causes of death (ICD-IX 001-999); natural causes of death (001–799); cancer (140–208); lung cancer (162); cardiovascular diseases (390–459); and respiratory diseases (460–519).

For SES, an indicator developed in Italy within a project supported by the Ministry of Health (Caranci et al. 2010) was used. This is a composite indicator, based on 2001 census data, combining the following five variables representing the multidimensionality of the social and material deprivation concept: low level of education, unemployment, non-homeowners, one parent families, and housing overcrowding. This index is also classified in quintiles, and the percentage of the population classified in the category reflecting the lowest SES (Table 1) was used here as a deprivation index for each neighbourhood.

Three different predictors were considered for evaluating population exposure to industrial site emissions: (1) the distance between the central point of the industrial site and the centre of the neighbourhood; (2) and (3) SO_2 and PM_{10} values at the ten neighbourhood centres. To estimate these two latter predictor values, air pollutant data available for the period 2006–2010 from seven air quality monitoring city stations plus two located near towns (Statte and Massafra) (Fig. 1) were used. Due to the unavailability of a continuous series of data, Massafra station was excluded. SO_2 and PM_{10} predictors at the ten neighbourhood centres were calculated using inverse quadratic distance weights.

Linear correlation among the four predictors (SES, distance, SO_2 and PM_{10}) was investigated by means of Pearson's coefficient.

Heterogeneity of ADR among neighbourhoods was investigated within a meta-regression framework (Dadvand et al. 2013; Greenland 1987; Thompson and Sharp 1999). Sex-specific analyses were conducted for each cause of

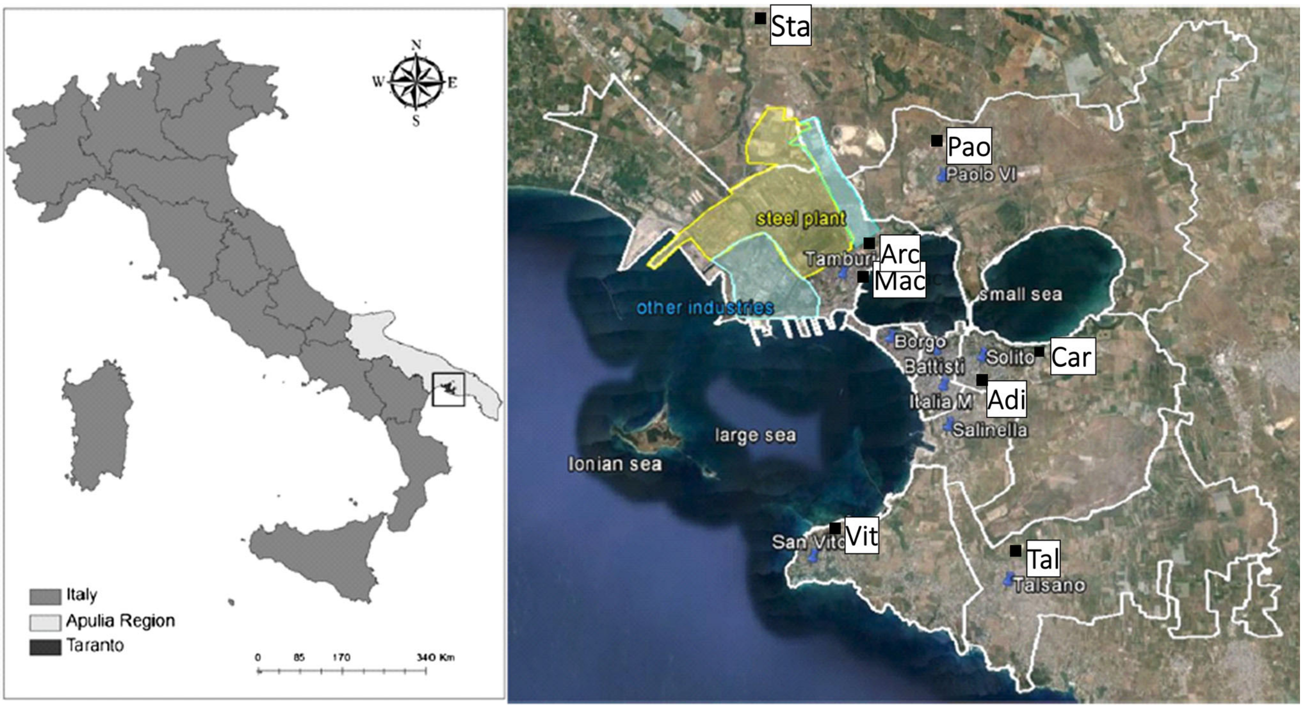

Fig. 1 Emission sources and monitoring stations. Taranto, Italy (2016)

Table 1 Neighbourhood populations and predictors used in the analysis

Neighbourhoods	Population	Distance from the industrial site (km)	SES (% of highest deprivation)[a]	PM_{10} (μg/m^3)[b]	SO_2 (μg/m^3)[b]
Paolo VI	19,811	5.6	64.3	30.1	4.0
Tamburi	28,692	1.7	69.4	32.0	2.7
Borgo	34,840	3.6	51.3	30.2	2.5
Tre Carrare Battisti	34,577	5.2	53.4	27.0	1.6
Solito Corvisea	30,854	6.8	17.6	26.1	2.3
Italia Monte.ro	38,034	5.8	20.2	26.6	1.4
Salinella	26,742	6.8	40.5	26.5	1.5
S. Vito	21,330	10.1	0.6	23.9	1.3
Talsano	30,461	13.0	20.5	26.4	2.2
Statte	16,554	7.4	26.3	25.1	2.7

Taranto, Italy (1998–2010)

[a] 2001 Italian Census

[b] 2007–2010

death. The statistical significance of between-neighbourhood heterogeneity was tested using Cochran's Q test. Variance of effect estimates τ^2 were used to quantify the between-neighbourhood heterogeneity, and the I^2 statistic with 95 % confidence intervals (95 % CI) was used to estimate the proportion of total variation in effect estimates across neighbourhoods attributable to the between-neighbourhood heterogeneity (Higgins and Thompson 2002). DerSimonian and Laird random-effects models meta-analysis (DerSimonian and Laird 1986) was used and I^2 was classified as follows: <25 %, very low heterogeneity; 25–50 % low heterogeneity; 50–75 %, moderate heterogeneity; and >75 %, high heterogeneity (Higgins and Thompson 2002). A meta-regression analysis was performed with ADR being used as the dependent variable and a single predictor as independent variable. Outliers were detected by calculating studentized residuals (Pope 1976). In a second step, to control for SES in meta-regression models, we used SES and one of the other predictors as an independent variable and checked for multicollinearity through the variance inflation factor (VIF) (Belsley et al. 1980).

Meta-analysis and meta-regression were performed using the R statistical package (http://cran.r-project.org), with `metafor` and `meta` libraries. For the outlier analysis, we used the `car` package and the `outlier.test` command.

Results

Table 1 shows the values of the predictors used in the analyses for the ten neighbourhoods. SES percentage of highest deprivation, PM_{10} and SO_2 concentration values ranged from 0.6 %, 25.1, 1.3 μg/m^3 to 69.4 %, 32.0, 4.0 μg/m^3, respectively. Tamburi, the neighbourhood closest to the steel factory, showed the highest percentage of residents with very low socioeconomic status (69.4 %) and the highest mean value (32.0 μg/m^3) of PM_{10}. Paolo VI, a neighbourhood 5.6 km away from the industrial site, showed the second highest deprivation index (64.3 %) and the highest SO_2 concentration value (4.0 μg/m^3).

Figure 2 shows the spatial patterns of SO_2 and PM_{10} concentration values averaged over 2006–2010, derived from series of measurements from the local ground stations. The differences in the spatial distribution of the two pollutants, computed for the ten neighbourhoods, are displayed as continuous fields. The PM_{10} distribution was characterised by high values around the industrial site, with decreasing concentration values as distance from the source increased. SO_2 concentration values were highest some kilometres away from the emission sources in the NE direction, and showed minimum values closer to the town with a gradient along the SW to NE direction.

ADR varied across neighbourhoods and according to cause of death (Table 2). High heterogeneity between neighbourhoods (I^2 values in Table 3) was registered for total (89.6 % among males and 90.1 % among females) and natural causes of death (84.7 % among males and 85.3 % among females) (Table 3). Low or very low heterogeneity between neighbourhoods was observed for lung cancer (0.0 % among males and females), for cancer (51.4 % among males and 27.3 % among females) and respiratory diseases (36.5 % among males and 42.3 % among females), and for cardiovascular causes of death among males (45 %) (Table 3).

Table 4 shows Pearson's coefficient values computed among predictors. They varied from 0.29 to 0.88 as

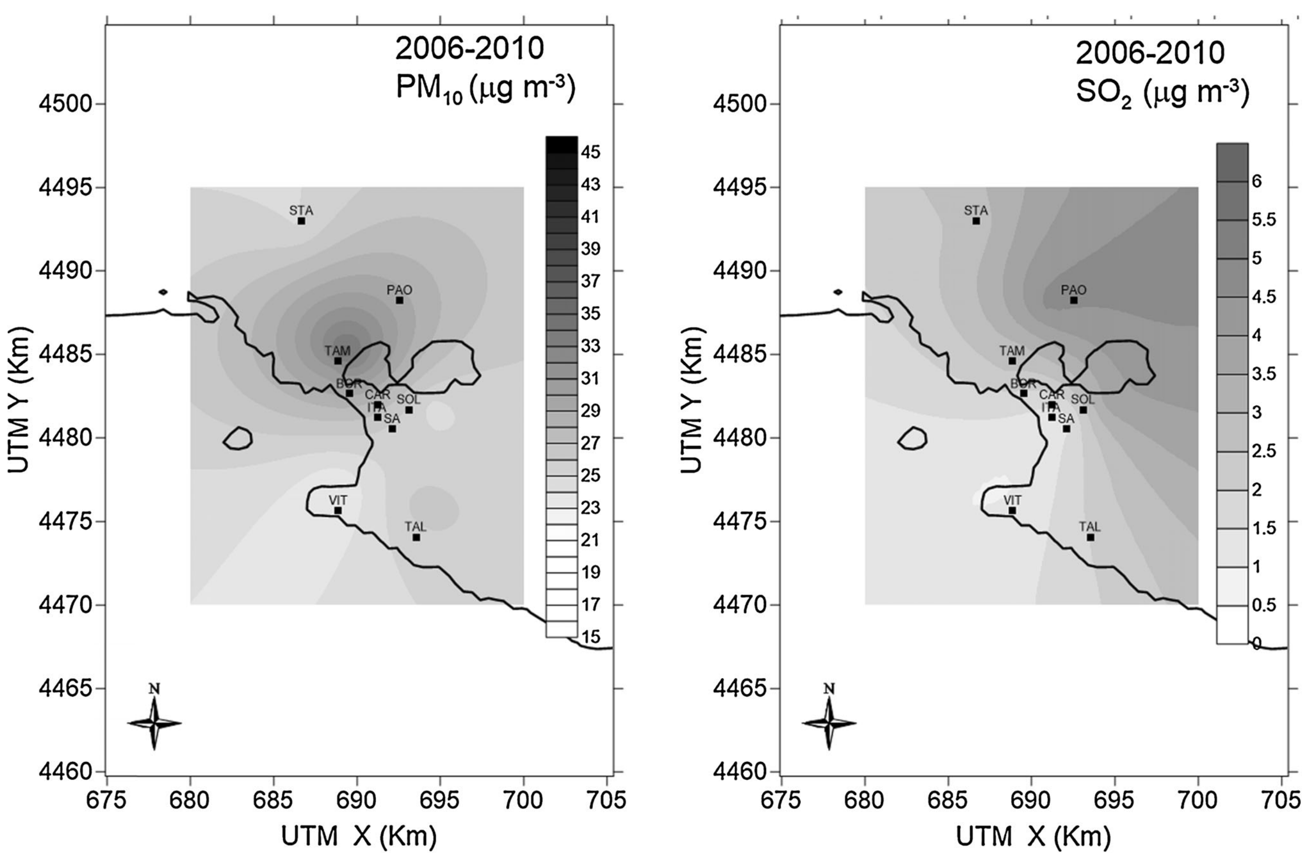

Fig. 2 Spatial pattern of SO_2 and PM_{10}. Taranto, Italy (2006–2010)

Table 2 Direct age-adjusted death rates (ADR per 100,000 inhabitants) according to cause of death, neighbourhoods, and sex

Neighbourhoods	Causes of death (ICD-IX)					
	All-causes (001–999)	Natural causes (001–799)	Cancer (140–208)	Lung cancer (162)	Cardiovascular (390–459)	Respiratory (460–419)
Males						
Paolo VI	1152	1109	390	166	350	138
Tamburi	1080	1014	363	117	335	104
Borgo	990	937	316	97	318	98
Tre Carrare Battisti	934	884	300	96	300	89
Solito Corvisea	902	864	298	95	290	95
Italia Monte.ro	877	823	283	93	287	76
Salinella	870	830	328	104	259	88
S. Vito	835	833	297	80	293	78
Talsano	888	855	317	102	269	78
Statte	949	816	297	101	261	122
Females						
Paolo VI	774	746	192	19	268	46
Tamburi	665	629	139	10	274	42
Borgo	604	564	159	13	220	44
Tre Carrare Battisti	604	579	170	13	220	40
Solito Corvisea	553	536	161	10	207	29
Italia Monte.ro	538	512	150	15	199	31
Salinella	559	547	171	10	209	35
S. Vito	594	576	173	13	233	42
Talsano	557	556	145	11	229	29
Statte	596	533	138	8	219	46

Taranto, Italy (1998–2010)

absolute values. Negative correlation coefficients were observed between distance from the industrial site and the other variables. Low socioeconomic status and PM_{10} were positively associated (0.88) and negatively associated with distance from the industrial site (−0.74 and −0.73, respectively).

Table 5 shows the meta-regression coefficients obtained from regression models using as dependent variables ADR only for those causes of death for which high heterogeneity between neighbourhoods was detected. Mortality increased with the percentage of population classified with the highest level of deprivation and air pollutant concentrations, decreasing with increasing distance from the steel industry (Table 5 and Figure S1 in the supplementary material). Generally, the predictors explain only part of the heterogeneity. In fact, evidence of nonzero between-neighbourhood heterogeneity (τ^2) was found (Table 5). Among males, the analysis showed Paolo VI as an outlier in models with SES, distance, and PM_{10} as predictors (Table 5; Figures S2–S4), and among females this neighbourhood emerged as an outlier for all predictors (Tables 5, 6).

After accounting for SES in the regression models, moderate heterogeneity between neighbourhoods was still detected for all-causes of death, for both males and females (58.4 % among males and 72.8 % among females) (Table S2).

Regression models with two variables, i.e., SES and one other predictor, showed SO_2 to be the only significant predictor (regression coefficient: 69.3 confidence interval (38.0; 100.7) and 52.2 (4.1; 100.3) among males and females, respectively) (Table S1); the lowest multicollinearity was detected in the model with SES and SO_2 (VIF = 2 both for males and females), and the highest multicollinearity was detected in the model with SES and PM_{10} (VIF = 4.5 both for males and females) (Table S1).

Discussion

Investigating the heterogeneity of mortality due to various causes between neighbourhoods in Taranto our findings indicated that SES, PM_{10}, and SO_2 are predictors of mortality measured at an ecological level. However, some

Table 3 Combined random-effects direct age-adjusted death rates (ADR per 100,000 inhabitants) and corresponding indicators of between-neighbourhood heterogeneity

Cause of death (ICD-IX)	Combined estimate	Heterogeneity		
	ADR (95 % CI)	τ^2	*p* value	I^2 (95 % CI)
Males				
All-causes (001–999)	942 (890; 996)	6510	<0.0001	89.6 % (80.3; 97.7)
Natural causes (001–799)	890 (842; 937)	4792	<0.0001	84.7 % (71.6; 97.0)
Cancer (140–208)	313 (298; 329)	318	0.0102	51.4 % (12.4; 91.1)
Lung cancer (162)	99 (93; 105)	0	0.0689	0.0 % (0.0; 93.7)
Cardiovascular (390–459)	294 (280; 309)	239	0.0280	45.0 % (0.0; 89.2)
Respiratory (460–419)	91 (84; 99)	52	0.0319	36.5 % (0.0; 91.8)
Females				
All-causes (001–999)	600 (564; 635)	2866	<0.0001	90.1 % (81.5; 98.0)
Natural causes (001–799)	571 (540; 603)	2091	<0.0001	85.3 % (73.4; 97.4)
Cancer (140–208)	157 (149; 165)	41	0.0790	27.3 % (0.0; 87.4)
Lung cancer (162)	12 (10; 14)	0	0.7092	0.0 % (0.0; 62.2)
Cardiovascular (390–459)	225 (211; 238)	328	0.0002	71.0 % (42.4; 93.1)
Respiratory (460–419)	37 (33; 41)	17	0.0490	42.3 % (0.0; 83.7)

Taranto, Italy (1998–2010)

Table 4 Correlation matrix of pre-specified predictors, Pearson coefficient

Predictor	Distance from industrial site	SES	PM_{10}	SO_2
Distance from industrial site	1	−0.74	−0.73	−0.29
SES	−0.74	1	0.88	0.57
PM_{10}	−0.73	0.88	1	0.61
SO_2	−0.29	0.57	0.61	1

Taranto, Italy (1998–2010)

important differences between predictors emerged. First, low SES and high PM_{10} concentrations are correlated, thus producing multicollinearity when applied together in regression models. Second, the analysis of outliers indicated that mortality levels in Paolo VI were out of the range of the values predicted using models with PM_{10}, distance and SES. Third, models with SO_2 were better for males at predicting Paolo VI levels of mortality.

Since concentrations of SO_2 and PM_{10} are mainly attributed to industrial activities (Gariazzo et al. 2007), our findings suggest the existence of two exposure patterns:

(a) a *proximal pattern*, based on the exposure to PM_{10} and affecting residents close to the industrial site;
(b) a *distal pattern*, based on SO_2 exposure and affecting residents further away from the industrial site.

This suggestion is supported by the analysis of outliers and by the different patterns in SO_2 and PM_{10} concentration values. In fact, Fig. 2 shows two different distributions of SO_2 and PM_{10} concentrations in the city, which might be explained by the different emission sources. This is in line with previous work of our research group (Mangia et al. 2013) which showed that various parts of the city are affected differently by the various emission sources depending upon meteorological conditions. The industrial site comprises more than 300 chimneys of heights varying from a few metres up to 210 m, emitting different quantities of different chemical composition. In particular, PM_{10} is emitted from chimneys up to 50 m in height, while SO_2 is emitted from chimneys over 100 m high (Gariazzo et al. 2007). Fugitive emissions are estimated to be responsible for more than 2000 tonnes of dust (Sanna et al. 2012). Being released at different quotas, the various contaminants are affected by different weather-diffusive conditions, and therefore, they may impact different areas. Given the type of emission surface, the dispersion of PM_{10} mainly impacts neighbourhoods, such as Tamburi, close to the plant and the mineral park. In contrast, the dispersion of SO_2 emitted mainly by taller stacks, impacts neighbourhoods at larger distances from the plant.

On one hand, linear correlation analysis showed that SES distance and PM_{10} are correlated and may confound their relative role in association with negative health outcomes. On the other hand, SO_2 is less correlated with SES, PM_{10}, or distance from the industrial site and may be associated with a different spatial exposure pattern originating from different sources of pollution subjected to different atmospheric dispersion modes.

Table 5 Meta-regression coefficients of models with one predictor, between-neighbourhood residual heterogeneity, and analysis of outliers

Predictors	Regression coefficient (95 % CI)	Residual heterogeneity		Analysis of outliers	
		τ^2	*p* value	Studentized residuals	*p* value
Cause of mortality (ICD-IX)					
Males					
All-causes (001–999)					
SES	3.3 (2.0; 4.6)	1073	0.0021	Paolo VI	0.0307
Distance	−17.8 (−30.6; −5)	2991	<0.0001	Paolo VI	0.0077
PM_{10}	29.8 (20.7; 38.8)	266	<0.0001	Paolo VI	0.0114
SO_2	104.4 (62.7; 146.1)	1156	0.0018	Tamburi	0.7459
Natural causes (001–799)					
SES	2.8 (1.5; 4.1)	762	0.0088	Paolo VI	0.0138
Distance	−14.3 (−26.3; −2.2)	2386	<0.0001	Paolo VI	0.0048
PM_{10}	27.0 (18.4; 37.7)	54	0.1162	Paolo VI	0.0010
SO_2	86.5 (41.4; 131.5)	994	0.0077	Statte	0.0119
Females					
All-causes (001–999)					
SES	1.9 (0.8; 2.9)	858	0.0006	Paolo VI	0.0023
Distance	−8.0 (−18.3; 2.3)	2118	<0.0001	Paolo VI	0.0014
PM_{10}	15.2 (4.3; 26.0)	1283	<0.0001	Paolo VI	0.0018
SO_2	15.2 (28.6; −94.3)	945	<0.0001	Paolo VI	0.0285
Natural causes (001–799)					
SES	1.6 (0.6; 2.5)	543	0.0011	Paolo VI	0.0038
Distance	−5.1 (−14.8; 4.6)	1781	0.3047	Paolo VI	0.0015
PM_{10}	12.9 (3.0; 22.9)	948	<0.0001	Paolo VI	0.0034
SO_2	51.1 (17.8; 84.5)	776	0.0009	Paolo VI	0.0718

Taranto, Italy (1998–2010)

Table 6 Regression of direct age-adjusted death rates (ADR per 100,000 inhabitants) for all-causes versus SES and one more predictor, variance inflation factor (VIF) for multicollinearity according to sex

Predictor/model	Male		Female	
	Regression coefficient (95 % CI)	VIF	Regression coefficient (95 % CI)	VIF
`ADR = a + b1*SES + b2*Distance`				
`a`	835.6 (688.1; 983.0)	2.2	489.7 (371.3; 608.0)	2.2
`b1`	3.1 (1.1; 5.3)		2.3 (0.7; 3.8)	
`b2`	−1.6 (−15.0; 15.7)		3.7 (−7.0; 14.3)	
`ADR = a + b1*SES + b2*PM`$_{10}$				
`a`	318.4 (−10.4; 647.1)	4.5	467.2 (27.6; 906.7)	4.5
`b1`	1.2 (−0.3; 2.7)		1.6 (−0.5; 3.7)	
`b2`	20.8 (7.3; 34.3)		2.5 (−15.8; 15.8)	
`ADR = a + b1*SES + b2*SO`$_2$				
`a`	716.0 (657.9; 775.1)	1.5	465.2 (415.0; 515.4)	1.5
`b1`	2.1 (1.2; 3.1)		1.0 (−0.8; 2.8)	
`b2`	69.3 (38.0; 100.7)		52.2 (4.1; 100.3)	

Taranto, Italy (1998–2010)

Some important limitations must be considered when interpreting the results of this study.

First, the mortality data we used refer to the period 1998–2010 and could include chronic exposure from before 1998. Thus, predictors based on the ambient concentration monitored during 2006–2010 could be irrelevant if the spatial patterns of the environmental stressors underlying the risk have changed. Nevertheless, comparisons between the concentration maps of SO_2 and PM_{10} patterns confirmed that spatial patterns persist over long time periods. Since the locations of the main emission sources and the relative emission intensities among different sources as well as the average meteorology and topography have not changed over the years, spatial air pollution patterns were not expected to be different.

We used meta-regression to explore sources of heterogeneity. Thus, the relationships described are observational associations (Thompson and Higgins 2002). Furthermore, given the limited number of observations (i.e. neighbourhoods), the potential to obtain robust conclusions is clearly limited.

Third, we used outcomes and predictors measures at an ecological level. This aspect must be taken into account when interpreting our results. In particular, we controlled our models for the SES variable computed at an ecological level, thus residual confounding cannot be excluded.

Conclusions

Our findings indicate that in the industrialised city of Taranto, most of the mortality heterogeneity between neighbourhoods could be explained by air pollution and SES. Two air pollution exposure patterns appear and need to be confirmed in further investigations. The two exposure patterns are both characterised by high mortality levels: a *proximal* one characterised by exposure to PM_{10} and a *distal* one characterised by exposure to SO_2. The former affects residents close to the industrial site and is largely associated with the extensive diffuse and fugitive emissions derived from the industrial site; the latter impacts residents at a distance downwind from the industrial site, and is likely associated with emission of pollutants from taller stacks (Mangia et al. 2013).

These results confirm that in the presence of a complex industrial site, evaluation of population exposure to air pollutants should take into account possible zones of influence of the various emission sources. In the specific case of Taranto, the analysis revealed that the influence of the industrial site on the city might be identified with PM_{10} and with SO_2, which although their concentration values in air are well below regulatory limits, could be used as a proxy of exposure to a more complex mixture of air pollutants emitted from industrial sources (Buringh et al. 2000; Wichmann et al. 2000). While the specific results and conclusions can be directly applied to the Taranto study area, the general concepts, the approach used, and some of the general trends identified are applicable to other industrialised urban areas.

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Compliance with ethical standards

This study did not receive any research grant.

Conflict of interest The authors declare no conflict of interest.

Ethical approval This article does not contain any studies with human participants or animals performed by any of the authors.

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