CHAPTER SIXTEEN

Relationships Between Heavy Metal Distribution and Cancer Mortality Rates in the Campania Region, Italy

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Contents

Abstract

We report geochemical and epidemiological data as maps representing the patterns of toxic metal concentrations and some, potentially, related pathologies in the Campania region of Italy. The comparison of a particular element distribution with specific pathologies, at regional scale, has been carried out taking into account previous epidemiological research, that demonstrated the existence of relationships between anomalous concentrations of some metals and incidence of some pathologies. This study shows that some types of cancer are found in Campania, in areas characterized by relatively high concentration of heavy metals, though, in epidemiological study, correlation does not automatically imply causation. For instance, Zn–Cd-rich areas overlap with areas of high prostate-cancer mortality; bladder and pancreatic cancer are correlated with Pb–Sb-rich areas, whereas, bronchial–tracheal–lung cancer is correlated with As-, Cd- and Pb-rich areas.

1. Introduction

An important factor to relate epidemiology with the presence of potentially toxic metals in the shallow environment, hence potentially bioavailable, is the accessibility of maps reporting territorial distribution of both toxic metals and organics and significant

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pathologies. Their representation constitutes a valid instrument to establish a correct comparison and to find interactions between element distribution in rocks, soils, and water and health of humans and other living organisms (Berger, 2003).

Illness history reflects the history of modifications which have occurred in the environment surrounding humans and living organisms. Environmental pollution has arisen mostly with the development of modern technologies and consequently, the diseases related to pollution have increased, but this linkage is often difficult to demonstrate on a cause–effect base. In fact, a purely geochemical approach to epidemiology study problem has the limitation in that correlation does not imply causation. Therefore, the fact that a correlation is observed between relatively high concentrations of some toxic metals (e.g., As, Pb, Cd, and others) in soils or sediments and a particular cancer type does not mean that these high metallic concentrations have any role in causing the cancer, or even that there is any increased probability that a specific toxic metal is a cause of the cancer.

In recent years, geo-medicine, a subsidiary of environmental medicine (Möller, 2000) which is born from the synergy between medicine and geology (Bølviken, 1998), studied the influence of environmental factors on the geographic distribution of the human and animal pathologies. Geo-medicine is, hence, important for public health and preventive medicine. Trace elements, as micronutrients—metals and nonmetals—are very important for human well-being, but the same elements have negative consequences on human health if they are ingested in anomalous amount (either in excess or in deficiency). Au2

The objective of this work, in particular, is to provide comprehensive geographic and geologic data to help understand possible interactions between the occurrence of anomalous amounts of toxic metal concentrations and pathologies in Campania region. The latter is, with Sardinia (De Vivo *et al.*, 1997, 2001, 2006c), the only Italian region covered by a systematic sampling of soils and stream sediments with the distribution of toxic metals.

At this stage of the study, no cause–effect relationships between toxic metal distribution and cancer rates can be established, as a joint study with medical and epidemiological professionals is needed to accurately interpret the epidemiological data available for the Campania region.

2. Geology, Geochemical Data, and Cancer Mortality Data of Campania Region

The lithologies of Campania region (Fig. 16.1) can be grouped into three domains:

(1) Mountainous sector represented by the Campanian Apennine Mountains, made up mostly by limestones and classified as a Neogenic Nappe edifice
(2) Plain sector made up by graben structures forming the Campanian Plain and other structures, where there is occurrence of pre-, syn-, and postorogenic sedimentation (mostly, fine-grained sediments)
(3) Volcanic sector made up by volcanics of the Neapolitan potassic province (Somma-Vesuvio, Campi-Flegrei, Ischia, and Roccamonfina) (Peccerillo, 2005).

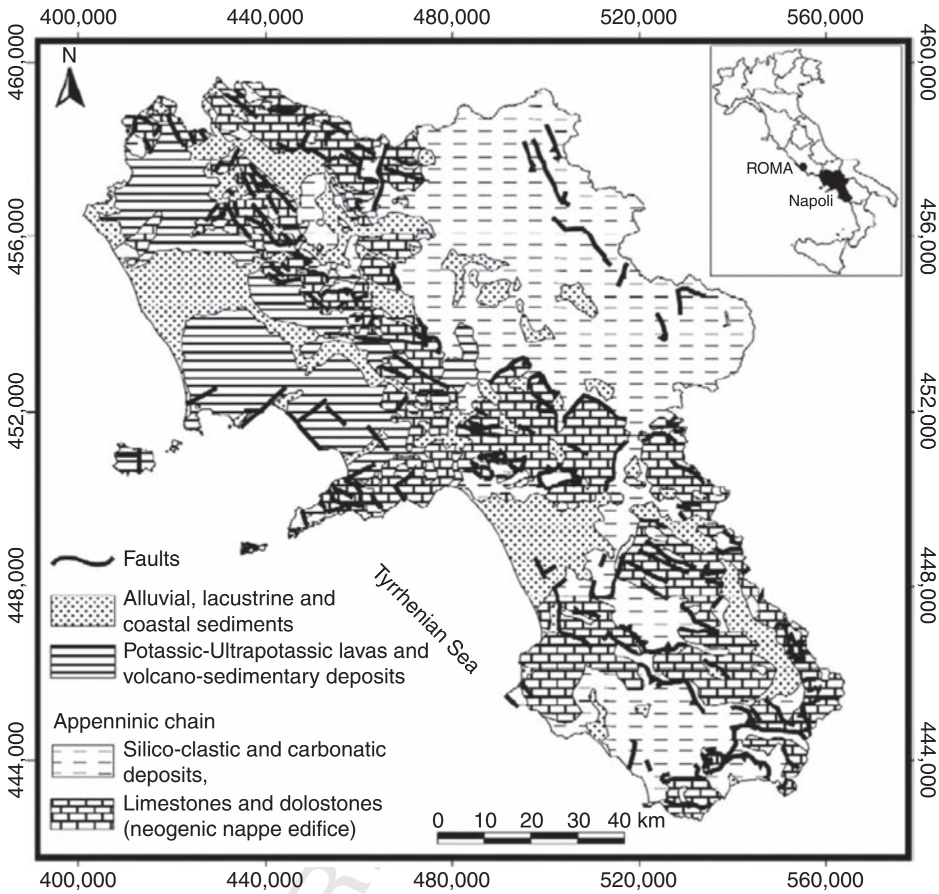

Figure 16.1 Simplified geologic map of the Campania region, Italy.

Geochemical data used for this study are chemical analyses of soil and stream sediment samples covering the entire Campania region (Albanese *et al.*, 2007; De Vivo *et al.*, 2006a, b). The Geochemical Atlases of Campania region (De Vivo *et al.*, 2006a) and of urban and provincial areas of Naples (De Vivo *et al.*, 2006b) include geochemical maps generated from chemical data from 2389 stream sediment and 982 soil samples. Samples were analyzed for 37 elements: Ag, Al, As, Au, B, Ba, Bi, Ca, Cd, Co, Cr, Cu, Fe, Ga, Hg, K, La, Mg, Mn, Mo, Na, Ni, P, Pb, S, Sb, Sc, Se, Sr, Te, Th, Ti, Tl, U, V, W, and Zn by ICP-MS and ICP-AES (inductively coupled plasma mass spectrometry and atomic emission spectrometry) at ACME Analytical Laboratories (Vancouver, Canada).

Specifically, for each sample, a 15-g split of pulp was digested in 45 ml of Aqua Regia (equal quantities of HCl, HNO_3, and distilled water) at 90 °C for 1 h. The solution was taken to a final volume of 300 ml with 5% HCl. Aliquots of sample solution were aspirated into a Jarrel Ash Atomcomp 975 ICP-AES and a Perkin Elmer Elan 6000 ICP-MS instruments.

Precision of the analysis was calculated using three in-house replicates, and two blind duplicates submitted by the authors. Accuracy was determined using ACME's in-house reference material, DS2 (HMTRI, 1997) (Table 16.1).

Table 16.1 Detection limits, accuracy, and precision

Elements	Unit	Detection limit (DL)	Accuracy (%)	Precision (%RPD)
Al	%	0.01	0	1.8
Ca	%	0.01	3.9	2.2
Fe	%	0.01	0.7	1.3
K	%	0.01	6.3	5.3
Mg	%	0.01	0	1.5
Na	%	0.001	3.6	2.9
P	%	0.001	0	3.6
S	%	0.02	30	11.9
Ti	%	0.001	0	5.7
As	mg/kg	0.1	0.3	3
B	mg/kg	1	0	11
Ba	mg/kg	0.5	0.3	1.5
Bi	mg/kg	0.02	1.8	3.2
Cd	mg/kg	0.01	1.4	5.6
Co	mg/kg	0.1	0	2.7
Cr	mg/kg	0.5	1.5	3.2
Cu	mg/kg	0.01	1.6	3.7
Ga	mg/kg	0.1	3.2	2.2
La	mg/kg	0.5	3.5	3.4
Mn	mg/kg	1	0.5	1.9
Mo	mg/kg	0.01	1.2	3.1
Ni	mg/kg	0.1	0.6	1.7
Pb	mg/kg	0.01	0.6	3.5
Sb	mg/kg	0.02	1.2	3.1
Sc	mg/kg	0.1	0	4.4
Se	mg/kg	0.1	0	28
Sr	mg/kg	0.5	5.3	2.4
Te	mg/kg	0.02	0.9	8.4
Th	mg/kg	0.1	5.1	3.6
Tl	mg/kg	0.02	1	3.6
U	mg/kg	0.1	1.6	3.7
V	mg/kg	2	1.3	2.4
W	mg/kg	0.2	2.7	4.4
Zn	mg/kg	0.1	0.5	2.6
Ag	mg/kg	2	0.4	7.9
Au	μg/kg	0.2	4.8	28.9
Hg	μg/kg	5	0	8

RPD, relative percent difference.

For each sampled site, radioactivity was measured by a portable scintillometer (Lima *et al.*, 2005). The data set was used to produce various types of geochemical maps, including dot maps, baseline maps, factor analysis association maps, risk, partial and total radioactivity maps.

Mortality data for four groups of cancer, grouped per ASL (ASL are local health units), have been used for this study and they have been extracted from the Atlas of Cancer Mortality in Campania region in the period 1989–1992 (Montella *et al.*, 1996). Since the area of influence of each local health unit is established on the basis of population density, Campania region territory is divided into 13 ASL and 5 of them belong to the Neapolitan province. For each ASL, mortality data have been expressed as Regional Standard Mortality Ratio (SMR-REG). The SMR-REG, expressed as a percentage, is the ratio between the number of observed deaths from a defined cause for each considered ASL and the number of expected deaths (expected deaths REG) computed on the basis of the population sorted per age group in each ASL and the regional age-specific mortality rates (Table 16.2).

To calculate the number of expected deaths for each ASL, the following formula has been used:

$$\text{Expected deaths REG} = \sum\nolimits_i \mathrm{Tr}_{i*} p_i$$

where Tr_i = regional age-specific mortality rates calculated for 100,000 in population for the i-esim age group referred to the average four calendar years considered (1998–2001) and p_i= ASL population in the i-esim age group.

To take into account the uncertainties of mortality data, a 95% confidence interval (CI) has been calculated for each SMR-REG using the following formula

$$\mathrm{CI} = \mathrm{SMR} \pm 1.96\mathrm{SE}$$

where SE = standard error of SMR = square root of [SMR(1 - SMR)]/P and P = total ASL population.

SMR values included within the lower and the upper limit of the CI have been assumed as equal. As consequence, if the value of 100 is included in the CI a nonsignificant difference occurs between the number of observed deaths and the expected death in a considered ASL. Otherwise, if the lower limit or the higher limit of the CI are respectively above or below 100, there is a 95% probability that observed deaths are significantly less or more than the expected ones.

3. Methods

To compare the epidemiological data with the distribution of toxic metals in the study area, geochemical data for 13 harmful elements (although some are micronutrients) (As, Cd, Co, Cr, Cu, Hg, Ni, Pb, Se, Sb, Tl, V, and Zn) from the complete geochemical database of De Vivo *et al.* (2006a, b) have been grouped and elemental average concentration values have been calculated for each ASL, as well (Fig. 16.2).

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Table 16.2 For each ASL and considered cancer type, for males and females, observed deaths, expected number of deaths, SMR-REG, and SE are reported

Males																
	Trachea, bronchus, and lung				Prostate				Bladder				Pancreas			
ASL	Observed deaths	Reg. expected deaths	SMR-REG	SE	Observed deaths	Reg. expected deaths	SMR-REG	SE	Observed deaths	Reg. expected deaths	SMR-REG	SE	Observed deaths	Reg. expected deaths	SMR-REG	SE
NA 1	1947	1505	129.4	2.9	598	499	119.8	4.9	391	310	126.1	6.4	156	129	120.9	9.7
NA 2	530	427	124.1	5.4	138	148	93.2	7.9	116	84	138.1	12.9	33	37	89.2	15.6
NA 3	434	348	124.7	6.0	100	104	96.2	9.6	89	65	136.9	14.4	37	30	123.3	20.5
NA 4	536	551	97.3	4.2	147	171	86.0	6.9	140	109	128.4	10.9	42	47	89.4	13.7
NA 5	969	874	110.9	3.6	287	288	99.7	5.9	201	177	113.6	8.0	73	75	97.3	11.4
CE 1	432	479	90.2	4.3	223	200	111.5	7.4	87	103	84.5	9.1	34	41	82.9	14.1
CE 2	644	605	106.4	4.2	187	111	168.5	7.6	120	122	98.4	9.0	56	52	107.7	14.4
SA 1	394	405	97.3	4.9	159	165	96.4	7.6	68	82	82.9	10.0	28	35	80.0	15.2
SA 2	671	750	89.5	3.5	227	256	88.7	5.9	126	160	78.8	7.0	67	65	103.1	12.6
SA 3	368	551	66.8	3.5	195	230	84.8	6.1	81	132	61.4	6.8	41	49	83.7	13.1
AV 1	208	373	55.8	3.9	153	165	92.7	7.5	56	90	62.2	8.3	30	33	90.9	16.6
AV 2	329	423	77.8	4.3	134	168	79.8	6.9	66	95	69.5	8.5	25	37	67.6	13.5
BN	391	562	69.6	3.5	261	234	111.5	6.9	119	130	91.5	8.4	57	49	116.3	15.3
Campania	7853	7853	100.0	—	2809	2739	102.6	—	1660	1660	100.0	—	679	679	100.0	—

Females												
	Trachea, bronchus, and lung				Bladder				Pancreas			
ASL	Observed deaths	Reg. expected deaths	SMR-REG	SE	Observed deaths	Reg. expected deaths	SMR-REG	SE	Observed deaths	Reg. expected deaths	SMR-REG	SE
NA 1	314	226	138.9	7.9	88	63	139.7	14.8	158	124	127.4	10.1
NA 2	70	57	122.8	14.6	14	15	93.3	24.9	39	30	130.0	20.8
NA 3	44	48	91.7	13.9	7	12	58.3	22.5	27	24	112.5	21.4
NA 4	63	74	85.1	10.8	20	19	105.3	23.3	38	39	97.4	15.9
NA 5	128	119	107.6	9.5	40	33	121.2	19.4	63	64	98.4	12.4
CE 1	62	63	98.4	12.4	15	18	83.3	21.7	27	35	77.1	14.9
CE 2	91	82	111.0	11.6	22	22	100.0	21.5	42	44	95.5	14.8
SA 1	50	55	90.9	13.0	13	15	86.7	24.5	32	29	110.3	19.3
SA 2	86	98	87.8	9.5	24	28	85.7	17.7	54	54	100.0	13.7
SA 3	48	69	69.6	10.1	13	21	61.9	16.8	32	39	82.1	14.3
AV 1	24	48	50.0	10.3	10	15	66.7	21.2	19	28	67.9	15.8
AV 2	53	58	91.4	12.6	10	17	58.8	18.4	22	32	68.8	14.4
BN	36	74	48.6	8.1	24	23	104.3	21.7	32	42	76.2	13.4
Campania	1069	1069	100.0	—	300	300	100.0	—	585	585	100.0	—

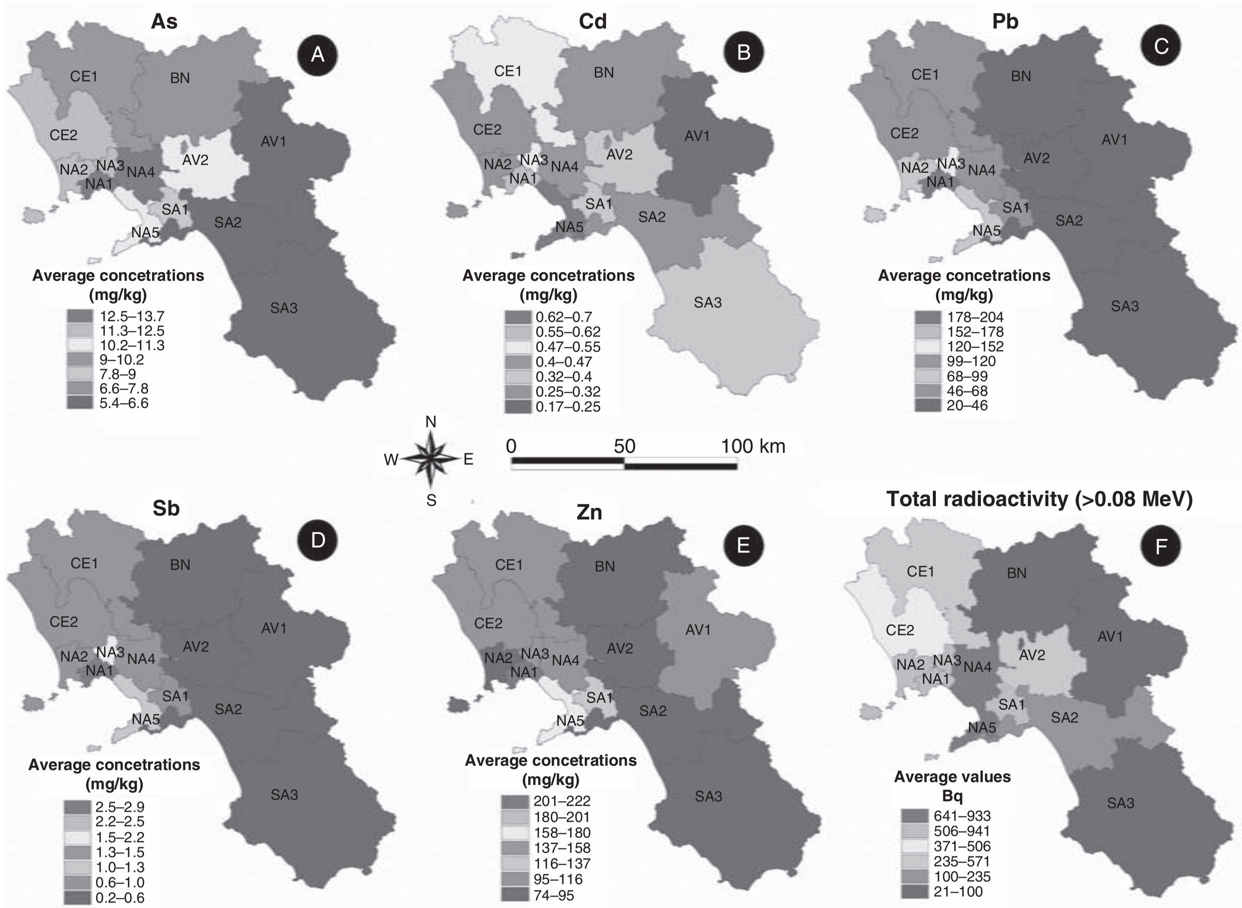

Figure 16.2 Average concentration maps of As (A), Cd (B), Pb (C), Sb (D), Zn (E), and total radioactivity (MeV > 0.08) (E) distribution in ASL territories.

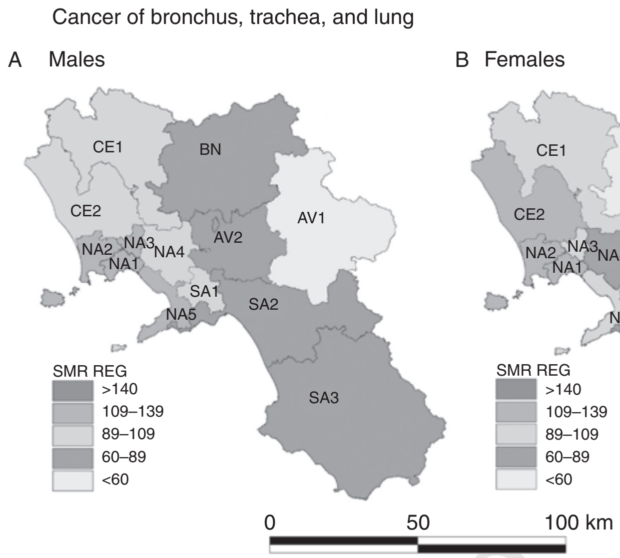

Figure 16.3 Maps representing the Regional Standardized Mortality ratio (SMR-REG) distribution for each ASL referred to bronchus, trachea, and lung neoplasm cancer, for male (A) and female (B) in Campania region. NA, AV, BN, CE, and SA prefix in the labels indicates the pertinence of an ASL to a provincial territory (NA = Naples; AV = Avellino; BN = Benevento; CE = Caserta; SA = Salerno).

Average concentrations of considered elements and SMR-REG data for various cancer types data have been mapped, by means of vector maps, handled with GIS software, representing ASL territories with polygons (Figs. 16.3–16.5). Basically, for each element, the geochemical map has been produced classifying polygons on the basis of the respective average concentrations whereas, for each considered cancer type, mortality maps have been produced classifying polygons on the basis of the respective SMR-REG.

In addition, based on the same mapping criteria, the maps for partial (K^{40}, Th^{232}, U^{238}) and total radioactivity have been compiled.

Since the average concentrations for the 5 ASL of the Naples province have been calculated exclusively on soil sample data whereas stream sediments samples have been used for the rest of the ASL, geochemical data from different media were not mixed in statistical analysis.

4. Discussion of Results

4.1. Cancer of trachea, bronchus, and lung

Cancers of the trachea, bronchus, and lung cause many deaths in both men and women in the Campania region. It is the leading cause of death for men and the third leading cause of death for women, after breast cancer. The map which report

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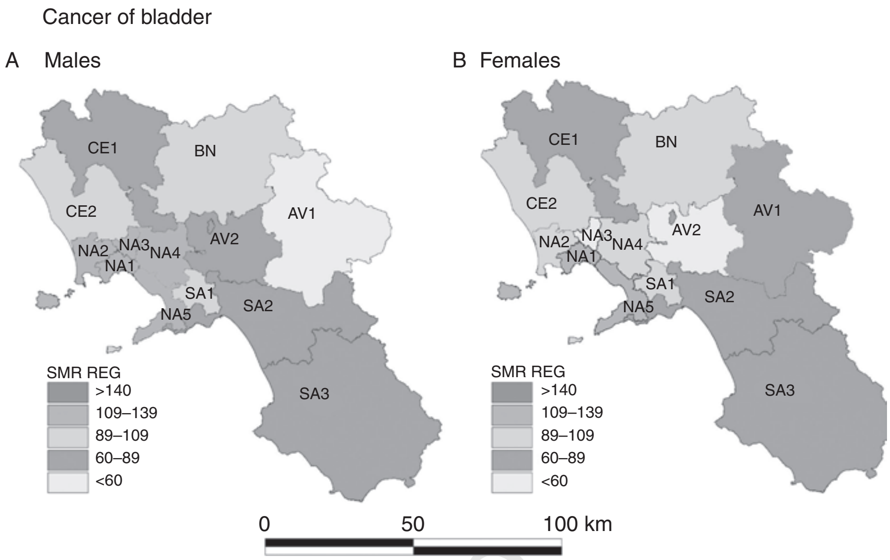

Figure 16.4 Map representing the SMR-REG distribution for each ASL referred to bladder cancer, for male (A) and female (B) in the Campania region. For explanations of labels, see Fig. 16.3.

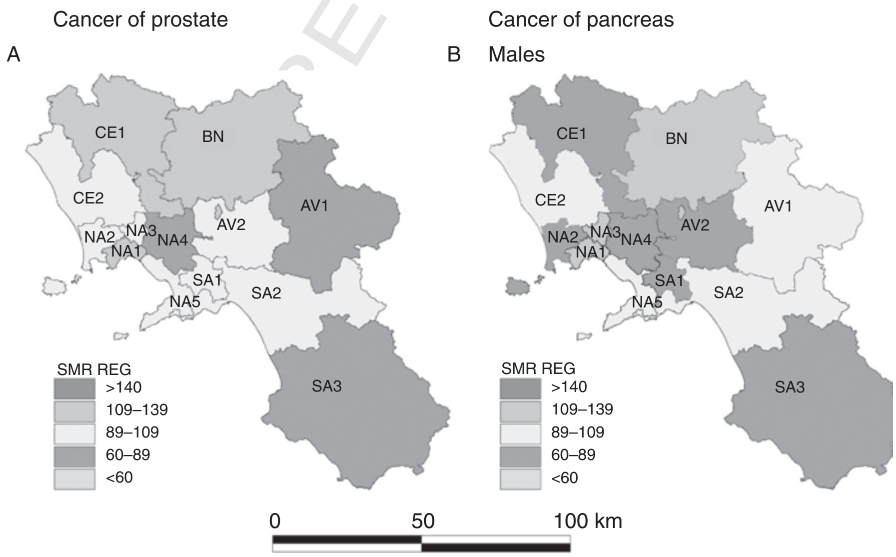

Figure 16.5 Map representing the SMR-REG distribution for each ASL referred to prostate cancer (A) and pancreatic cancer, for female (B), in Campania region. For labels explanations, see Fig. 16.3.

SMR-REG values for males (Fig. 16.3A) together with the observation of the respective SE show that mortality in 4 ASL of Naples province is, generally, significantly higher than regional average, whereas in Avellino, Benevento Salerno, and Caserta ASL deaths are equal or fewer than expected.

SMR-REG map generated for females (Fig. 16.3B) show an increase of mortality for the sole ASL NA1 (corresponding to the city of Naples) and SMR-REG values significantly below the regional average for ASL AV1, BN, and SA3.

The maps of average concentrations for As and Cd (Figs. 16.2A and B) show the highest values in correspondence of ASL territories of Naples and Caserta provinces. Lead shows high values only in the Naples province, especially in correspondence with ASL NA1 territory where the highest values for the SMR-REG for the cancer of trachea, bronchus, and lung are registered, as well. The Pb present in the urban area of Naples has been related principally with pollution from vehicular traffic (Cicchella *et al.*, 2005; De Vivo *et al.*, 2006b).

The correspondence between high SMR-REG and high anomalous values for As, Cd, and Pb mostly in Naples province represents a probability that a cause–effect relationship might exist between tracheal, bronchial, and lung cancer and toxic metal environmental pollution (Boyd *et al.*, 1970; Goyer, 1993). This hypothesis should be tested by means of biomonitoring data on blood and/or urine samples in residents of the Campania region.

Furthermore, in Campania, a roughly spatial correspondence has been found between the highest values of SMR-REG for lung cancer (in Naples and Caserta provinces) and the strong amount of gamma radiation emitted by the alkaline volcanics of the Neapolitan province (Fig. 16.2F). Since Rn gas, widely recognized as a cause of lung cancer (Field *et al.*, 2000), is a direct product of U^{238}decay process, in Naples and Caserta provinces, natural radioactivity can be considered a potential cause of the increased mortality for this cancer, though the spatial correspondence between SMR-REG and gamma radiation is not prima facie evidence in terms of a causative factor for the cancer.

4.2. Prostate cancer

The prostate is a gland present only in men, and produces prostatic liquid. The factors that influence the onset of prostate cancer are age, hormones, sexual activity, virus, genetic factors, and chronic exposure to Zn and Cd (Dinse *et al.*, 1999; Plant and Davis, 2003; Smith, 1999). Mortality in ASL NA1 (corresponding to the city of Naples), CE1, and BN (corresponding to the whole provincial territory of Benevento) are significantly higher than the regional average (Fig. 16.5A). Zinc is an element strongly correlated to prostate function because it is normally present in the prostatic gland to maintain its vitality; it can determine the weakening of immunity system and an antagonism with Se and Cu, increasing cancer risk (Bertholf, 1981). The Zn concentration map (Fig. 16.2E) shows the highest concentration values in the Naples urban area, where the highest SMR-REG values are found as well. The Cd concentration map (Fig. 16.2B), like Zn, presents higher values in Naples province (especially ASL NA5 and NA1), and subordinately in ASL CE1.

4.3. Bladder and pancreatic cancer

The bladder is an organ that accumulates urine via the ureters from the kidneys. For bladder cancer, there are some factors of risk, such as smoking, occupational exposure to toxic agents (i.e., toxic metal concentrations), use of particular medicines, and bacterial infections (Zeegers *et al.*, 2004). The pancreas is a gland that produces insulin and others enzymes necessary for digestion. Factors of risk for pancreatic cancer are smoking, some occupational exposures to industrial and agricultural solvents, and exposure to petroleum derivatives (Lowenfels and Maisonneuve, 2006). Both these cancers may be connected to Pb and Sb anomalous concentrations. The highest significant SMR-REG values for both cancer types (Figs. 16.4A and B, and 16.5B) are localized mostly in the Naples urban (ASL NA1) and provincial territory. The SMR-REG map generated for pancreatic cancer (Fig. 16.5B) shows an increase of mortality in correspondence with the Benevento province (ASL BN) where, locally, some elevated Zn values occur related to malfunctioning water and dust purification apparatus of local industries that use the metal to galvanize steel. Anthropogenic Pb and Sb values (Figs. 16.2C and D) are specially concentrated in the Naples urban territory (ASL NA1).

5. Conclusions

Maps of geochemical and epidemiological data in Campania region indicate some correlation between concentrations of some toxic metals and specific cancers, whose SMR-REG is above the regional standard value. The most evident correlations occur in the Naples urban and provincial areas, where the highest mortality values for all types of cancer occur, and where there are also high concentrations of heavy metals from anthropogenic pollution. The latter factor is confirmed by the observation that specific cancers are mostly localized in the highly urbanized Naples areas (e.g., trachea, bronchus, and lung cancer). In less urbanized areas, mortality is equal to or much lower than the regional average. For the Campania region therefore, it is possible to state, that, in some areas, a good spatial correspondence occurs between high SMR-REG values and certain types of cancer, namely, between cancer of the bronchus, trachea, and lung and anomalous concentrations of As, Cd, and Pb; prostate cancer and anomalous Zn–Cd concentrations; and bladder and pancreatic cancer and anomalous Pb and Sb concentrations.

This preliminary study, with the limitations of the epidemiological method of not being able to establish and demonstrate a direct cause–effect relationship between pollution and pathologies, nevertheless suggests strong evidence that a compromised environment such as the urban and provincial areas of Naples has a very negative effect for human health. The results in this study could be the base for a joint environmental geochemistry and epidemiological study whose aim would be to provide scientifically sound information to local and national health and environmental authorities with the hope of improving the quality of the environment and human health in the highly urbanized areas of the Campania region.

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REFERENCES

Albanese, S., De Vivo, B., Lima, A., and Cicchella, D. (2007). Geochemical background and baseline values of toxic elements in stream sediments of Campania region (Italy). *J. Geochem. Explor.* **93,** 21–34.

Berger, A. R. (2003). Linking health to geology. *In* ''Geology and Health. Closing the Gap'' (H. C. Skinner and A. R. Berger, eds.), pp. 5–11. Oxford University Press, New York.

Bertholf, L. A. (1981). ''Zinc. Handbook on Toxicity of Inorganic Compounds.'' Marcel Dekker, New York, pp. 787–800.

Bølviken, B. (1998). Geomedisin (Geomedicine—in Norwegian with an English summary). *In* ''Geographisk Epidemiologi'' (A. Aase, ed.), Norsk J. Epidemiol. 8/1, 29–39. Au5

Boyd, J. T., Doll, R., Foulds, J. S., and Leiper, J. (1970). Cancer of lung in iron ore (haematite) miners. *Br. J. Ind. Med.* **27,** 97–103.

Cicchella, D., De Vivo, B., and Lima, A. (2005). Background and baseline concentration values of elements harmful to human health in the volcanic soils of the metropolitan and provincial areas of Napoli (Italy). *Geochem. Explor. Environ. Anal.* **5,** 29–40.

De Vivo, B., Boni, M., Marcello, A., Di Bonito, M., and Russo, A. (1997). Baseline geochemical mapping of Sardinia (Italy). *J. Geochem. Explor.* **60,** 77–90.

De Vivo, B., Boni, M., and Costabile, S. (2001). Cartografia geochimica ambientale della Sardegna. Carte di intervento per l'uso del territorio. *In* ''Monografia Memorie Descrittive della Carta Geologica d'Italia'' (B. De Vivo and M. Boni, eds.). Servizio Geologico Nazionale LVII, 7–32. Au6

De Vivo, B., Lima, A., Albanese, S., and Cicchella, D. (2006a). ''Atlante geochimico-ambientale della Regione Campania.'' Aracne Editrice, Roma. ISBN 88-548-0819-9 pp. 216.

De Vivo, B., Cicchella, D., Lima, A., and Albanese, S. (2006b). ''Atlante Geochimico-Ambientale dei suoli dell'area urbana e della provincia di Napoli.'' Aracne Editrice, Roma. ISBN 88-548-0563-7 pp. 324.

De Vivo, B., Boni, M., Lima, A., Marcello, A., Pretti, S., Costabile, S., Gasparrini, M., Iachetta, A., and Tarzia, M. (2006c). Cartografia geochimica ambientale e carte di intervento per l'uso del territorio del Foglio Cagliari, Sardegna Meridionale. *In* ''Monografia Memorie Descrittive della Carta Geologica d'Italia'' (B. De Vivo, ed.). APAT-Servizio Geologico Nazionale, LXIX, 5–40. Au7

Dinse, G. E., Umbach, D. M., Sasco, A. J., Hoel, D. G., and Davis, D. L. (1999). Unexplained increased in cancer incidence in the United States from 1975 to 1994: Possible sentient health indicators? *Annu. Rev. Public Health* **20,** 173–209.

Field, R. W., Steck, D. J., Smith, B. J., Brus, C. P., Fisher, E. L., Neuberger, J. S., Platz, C. E., Robinson, R. A., Woolson, R. F., and Lynch, C. F. (2000). Residential radon gas exposure and lung cancer. The Iowa radon lung cancer study. *Am. J. Epidemiol.* **151,** 1091–1102.

Goyer, R. A. (1993). Lead toxicity: Current concerns. *Environ. Health Perspect.* **100,** 177–187.

HMTRI (Hazardous Materials Training and Research Institute) (1997). ''Site Characterization: Sampling and Analysis.'' Van Nostrand Reinhold, New York, USA. pp. 336.

Lima, A., Albanese, S., and Cicchella, D. (2005). Geochemical baselines for the radioelements K, U, and Th in the Campania region, Italy: A comparison of stream-sediment geochemistry and gamma-ray surveys. *Appl. Geochem.* **20,** 611–625.

Lowenfels, A. B., and Maisonneuve, P. (2006). Epidemiology and risk factors for pancreatic cancer. *Best Pract. Res. Clin. Gastroenterol.* **20**(2), 197–209.

Möller L. (ed.), (2000). *Environ. Med.* Joint industrial Safety Council, 333. Au8

Montella, M., Bidoli, E., De Marco, M. R., Redivo, A., and Francesci, S. (1996). ''Atlante della mortalità per tumori nella Regione campania, 1998–92.'' Lega Italiana per la Lotta contro i Tumori, Istituto nazionale tumori, Napoli, pp. 136.

Peccerillo, A. (2005). ''Plio-Quaternary Volcanism in Italy.'' Springer-Verlag, Berlin, pp. 361.

Plant, J. A., and Davis, D. L. (2003). Breast and prostate cancer: sources and pathways of endocrine-disrupting chemicals (ECS). *In* ''Geology and Health. Closing the gap'' (H. C. Skinner and A. R. Berger, eds.), pp. 95–98. Oxford University Press, New York.

Smith, S. K. (1999). Cadmium. *In* ''Encyclopedia of Geochemistry'' (C. P. Marshall and R. W. Fairbridge, eds.), Kluwer Academic Publishers, Dordrecht, The Netherlands, pp. 656.

Zeegers, M. P. A., Kellen, E., Buntinx, F., and Brandt, P. A. (2004). The association between smoking, beverage consumption, diet and bladder cancer: A systematic literature review. *World J. Urol.* **21**(6), 392–401.