Ann Ist Super Sanità 2017 | Vol. 53, No. 2: 108-117
DOI: 10.4415/ANN_17_02_06

ORIGINAL ARTICLES AND REVIEWS

Mortality of populations residing in geothermal areas of Tuscany during the period 2003-2012

Elisa Bustaffa[1], Fabrizio Minichilli[1], Daniela Nuvolone[2], Fabio Voller[2], Francesco Cipriani[2] and Fabrizio Bianchi[1]

[1]*Unità di Epidemiologia Ambientale e Registri di Patologia, Istituto di Fisiologia Clinica, Consiglio Nazionale delle Ricerche, Pisa, Italy*
[2]*Osservatorio di Epidemiologia, Agenzia Regionale di Sanità della Toscana, Florence, Italy*

Abstract

Introduction. The limited scientific knowledge on the relationship between exposure and health effects in relation to geothermal activity motivated an epidemiologic investigation of Tuscan geothermal area.

Aim. This study aims at describing mortality of populations living in Tuscan municipalities in the period 2003-2012.

Method. Sixteen municipalities were included in the study area: eight in the northern and eight in the southern area. Mortality data come from the Regional Mortality Registry of Tuscany. Fifty-four causes of death, considered of interest for population health status or consistent with "Project SENTIERI" criteria, are analyzed.

Results. Results show a worse mortality profile in the southern area, especially in males, for whom excesses of all cancers and some causes of cancer emerge, while in the northern area an excess of cerebrovascular diseases among females merits attention. Further and more appropriate studies are needed to clarify the etiology of some diseases and to better assess a potential cause-effect relationship.

Key words
- geothermal
- mortality
- health
- epidemiology

INTRODUCTION

Geothermics studies the production and the transfer of heat that originates in the earth's crust following the decay of radioactive isotopes [1, 2]. Volcanoes, geysers, fumaroles and hot springs are all natural visible manifestations of this thermal energy contained in the earth. Geothermal areas are characterized by geological conditions that allow a vector (water in liquid or gas phase) to transport heat from a thermal source to the surface. Electricity production is the most important use of conventional geothermal resources at high temperature (> 150 °C), as in the case of geothermal areas of Tuscany. For the production of electric energy the geothermal fluid is extracted from deep wells and then re-injected through appropriate wells.

The environmental impact caused by the exploitation of geothermal energy has recently become subject of further investigations. Geothermal plants for energy production promote the transportation to the surface of fluids with emission in the atmosphere of vapors gases and pollutants that can reach concentrations higher than those of natural emissions [3].

Emissions from geothermal plants in Tuscany consist of steam and gases released through cooling towers and, once condensed, they are reinjected while sludge is disposed in landfills. Gas emissions in air are mostly composed of carbon dioxide (CO_2) (85.4%), hydrogen sulfide (H_2S) (1-2%) and methane (CH_4) (0.4%) [3]. Nitrogen, hydrogen, ammonia, boric acid, radon, rare gases and volatile forms of trace elements such as mercury, arsenic and antimony are emitted to a lesser extent [3]. In addition to pollutant emissions, geothermal exploitation may be accompanied by subsidence problems, landscape damages, and interference with natural seismicity, noise pollution for plant workers and residents in the proximity of the plants.

To date studies on populations residing in geothermal areas are still scarce: seven studies were conducted in Rotorua (New Zealand) [4-6, 10-13] and one in Hawaii [7]. Rotorua is located in the active volcanic area of Taupo, characterized by one of the largest communities in the world exposed to geothermal emissions. In the Seventies, monitoring surveys showed a quarter of the population exposed to H_2S above 200 µg/m^3, with peak concentrations above 1.500 µg/m^3. It should be noticed that World Health Organization (WHO) now

Address for correspondence: Elisa Bustaffa, Unità di Epidemiologia Ambientale e Registri di Patologia, Istituto di Fisiologia Clinica, Consiglio Nazionale delle Ricerche, Via Moruzzi 1, 56124 Pisa, Italy. E-mail: elisa.bustaffa@ifc.cnr.it.

indicates a guideline value for H_2S of 150 µg/m³ (24-h average) [8] and tolerable concentrations for short-term and for medium-term exposure of 100 µg/m³ (on a period of 1-14 days) and 20 µg/m³ (on a period of 90 days), respectively [9]. Bates *et al.* conducted five out of the seven studies led in Rotorua. Three ecological studies revealed statistically significant excesses of respiratory system diseases among Maori women [4], an elevated rate of nasal cancer (based on four cases) [5] and increasing trends with increasing exposure for neurological causes of respiratory and cardiovascular diseases among the entire population [6]. On the other hand two analytical studies reported no association between H_2S exposure and asthma symptoms [11], lung function and Chronic Obstructive Pulmonary Diseases (COPD) [13].

With regard to studies in Rotorua not performed by Bates *et al.*, a study revealed significant clusters of respiratory disease cases, of asthma and of COPD [10], and an analytical study reported no association between H_2S exposure and cognitive function [12].

The only study not conducted in Rotorua investigated two communities living in areas prone to H_2S exposure, due to a geothermal power plant in Puna (Hawaii) and an industrial plant in Odessa (Texas). Odessa is characterized by an annual average concentration of H_2S in the range 3-40 µg/m³ and a daily maximum concentration of 150-300 µg/m³ while Puna by low values of H_2S (µg/m³), with occasional peaks. Authors observed greater risks for symptoms of central nervous system, for respiratory symptoms and for haematological disorders [7].

To date, these epidemiological studies on population exposed to geothermal emissions suggest a possible association between exposure to H_2S and health outcomes affecting the central nervous system and the respiratory system. Designs of the studies actually carried out are not sufficient to highlight a causal relationship between exposure and effect.

In 2012, we carried out an ecological study aimed to describe, in the period 2000-2006, the health status of populations living in Tuscan municipalities where concessions for exploitation of geothermal resources were granted [14]. The study is focused on the geothermal areas of Tuscany, between Pisa, Siena and Grosseto provinces. In these areas, geothermal resource has been exploited for a long time in order to produce electric energy and, to a smaller extent, in order to heat dwellings. Geothermal activities are present in central-southern Tuscany, the metalliferous hills and the Amiata massif, where two main areas are identified:

- the Amiata Mountain area (named hereafter "Southern Area") consists of 8 municipalities (Abbadia San Salvatore, Arcidosso, Castel del Piano, Piancastagnaio, Radicofani, Roccalbegna, San Casciano dei Bagni, Santa Fiora). This area is rich in thermal springs used for healing purposes and recreation. The sulfur springs are accompanied by the issue of H_2S in the atmosphere and, in the case of hot water, even mercury vapor [15]. Since the end of 1800 this area hosted a thriving mining of cinnabar (mercury sulfide-HgS), utilized for the production of metallic mercury. In this area there are still many decommissioned plants, evidence of past activity, whose decline began in the years 1960-1970. When the study began, in this area there were 5 plants with an installed total capacity of 88 MWe;
- the traditional area (named hereafter "Northern Area") consists of 8 municipalities (Castelnuovo Val di Cecina, Chiusdino, Montecatini Val di Cecina, Monteverdi Marittimo, Monterotondo Marittimo, Montieri, Pomarance, Radicondoli). In this area, where in XIX century the commercial exploitation of lagoons for production of boric acid started, thermal baths are few, but manifestations of endogenous gas rich in CO_2 and H_2S are widespread. Since then, the use of geothermal fluids has undergone a progressive increase. When the study began, in this area there were 27 plants with a total capacity of 764.5 MWe.

In these areas, both Regional Agency for the Environmental Protection of Tuscany (ARPAT) and Italian National Electricity Authority (ENEL) Green Power constantly monitor air quality, covering both the geothermal area and the towns affected by the geothermal plant emissions. The historic performance of H_2S concentrations in the air, as annual averages (µg/m³), recorded from 2010 to 2012 in geothermal areas of Tuscany, shows a general improvement. The geothermal area of Amiata, in the Province of Grosseto, presents lower values, during 2010-2011-2012 (2.99-1.99-1.11 µg/m³, respectively) compared to other Tuscan geothermal areas (22.95-27.66-15.72 µg/m³) [16].

Objectives of the study

The present study was carried out in the same areas defined in the previous study [14], in order to describe mortality in the population residing in the geothermal areas of Tuscany in the period 2003-2012, and to generate hypotheses for promoting further etiological epidemiological investigations.

MATERIALS AND METHODS

The population residing in the geothermal area in the period 2003-2012 was considered. The average resident population from 01-01-2003 to 12-31-2012 was 40 461 subjects, 19 678 men and 20 784 women. The population of the Southern Area accounted for 58.9% of the whole area.

Mortality causes. Data come from the Tuscan Regional Mortality Register and are classified according to the IX International Classification of Disease (ICD-IX). The group of causes and specific causes analyzed in this study are reported in *Table 1*.

Statistical methods. Statistical analysis was conducted by the following aggregated areas:

- Northern Area (named hereafter NoA);
- Southern Area (named hereafter SoA);
- Geothermal Area (Northern Area plus Southern Area, named hereafter GeA).

In order to calculate the expected events in the study areas, the mortality rates of both regional and sub-regional population were used as reference figures. The sub-regional area included 98 municipalities having the geographical coordinates of the main town falling in a 50 km radius from the edge of the study area. The radius of 50 km was chosen with the purpose of having

a large area with socio-economic and cultural characteristics more similar to the study area than the whole region (the study area accounted for 7% of the sub-regional area). Those towns with a population above 50 000 inhabitants were excluded from the sub-regional reference area to avoid the inclusion of subpopulations with environmental and socio-economic characteristics dissimilar from the reference area.

Standardized Mortality Ratios (SMRs) by age and Deprivation Index (DI) classes were calculated for total mortality and all causes of death for women, men, and both gender. The Confidence Interval (CI) was calculated using the Byar's approximate method [17]. To adjust the SMRs by socio-economic status, the DI proposed by Caranci was used [18].

For causes of death with a number of observations less than 3, SMRs are not reported in *Table 1*.

RESULTS

In the GeA, 6441 deaths (3111 males and 3330 females) occurred in the period 2003-2012: 38% of which among the 14 200 residents in the NoA (1188 males and 1256 females) and 62% among the 23 814 residents in the SoA (1923 males and 2074 females).

Table 1 shows DI-adjusted SMRs by area and gender for each cause or group of causes of death for the period 2003-2012.

Hereafter only statistically significant results or interesting results approaching but not reaching statistically significance will be discussed.

Considering all causes of death, the GeA shows an excess of mortality approaching but not reaching statistical significance only among males of + 3%. This excess is statistically significant in the SoA (+ 6%), particularly among males (+ 9%). Excesses in the SoA are significant both in the age classes 35-64 years and > 65 years. Concerning neoplasms in general (ICD-IX: 140-239), the SoA presents an excess of mortality of 10%, particularly among males (+ 16%). On the contrary, the NoA presents a number of deaths lower than expected (- 12%), particularly among males (- 14%). Among males within the GeA no statistically significant results for malignant diseases are observed but we highlight two interesting excesses approaching but not reaching statistically significance for malignant neoplasm of lip, oral cavity and pharynx and for liver. Among females, excesses of mortality for malignant neoplasms of ovary of + 38% and of the central nervous system of + 48%, and a statistically significant defect of mortality for malignant neoplasms of breast (- 23%) are observed. The NoA presents an excess of mortality among females of + 64% for malignant neoplasm of ovary and a defect of mortality among males of - 28% for malignant neoplasm of trachea, bronchus and lung. In the SoA we observe results for both gender. Among males, we notice excesses of mortality for malignant neoplasms of: i) stomach (+ 46%); ii) liver, gallbladder and bile ducts (+ 53%); iii) a defect of mortality for malignant neoplasm of lymphatic and hematopoietic tissue (- 31%) and iv) a not statistically significant excess for malignant neoplasm of lip, oral cavity and pharynx (+ 65%). Among females only an excess of mortality of + 84% for malignant neoplasm of the central nervous system and an interesting but not statistically significant excess for malignant neoplasm of stomach (+ 29%) are observed. We also observe two results that approach but not reach statistically significance for Parkinson's disease among males of the GeA and for senile and presenile organic psychotic conditions among females in the NoA.

Regarding diseases of the circulatory system (ICD-IX: 390-459) only the SoA presents a statistically significant result: a defect of mortality for both males and females of - 9% and - 7%, respectively. Within the group of cardiac diseases, in the areas we mainly observe defects of mortality in the areas. In fact, both GeA and SoA present defects of mortality for ischemic heart disease among both gender. Specifically, the GeA presents this defect of - 14% and of - 19% among males and females respectively, and the SoA of - 21% and of - 24% among males and females, respectively. The only excess of mortality is reported for cerebrovascular disease in the NoA among females (+ 15%).

For the diseases of the respiratory system in general (ICD-IX: 460-519), we observe excesses of mortality only among males in all the three areas. In the GeA the excess is of + 34%, in the NoA of + 32% and in the SoA of + 35%. We also report a not statistically significant excess among females of the SoA. Among diseases of the respiratory system all the three areas show excesses for pneumoconiosis among males: GeA of + 225%, NoA of + 264% and SoA of + 198%. GeA presents excesses among males for bronchopneumopathy chronic obstructive (+ 19%) while the SoA shows statistically significant excesses only among females for acute respiratory infections (+ 42%), specifically for pneumonia (+ 37%) and excesses approaching but not reaching statistical significance for the same diseases among males.

For the digestive system diseases (ICD-IX: 520-579) we report excesses of mortality among females of the GeA (+ 34%) and for both gender of the SoA (males + 27%; females + 47%). Among digestive system diseases we observe excesses of mortality for chronic liver disease and cirrhosis among females in the GeA (+ 48%) and for both gender in the SoA (males + 61%; females + 69%).

The SoA shows excesses of mortality not statistically significant for both gender for congenital anomalies (males + 156%; females + 143%) and statistically significant excesses for injury and poisoning among males (+ 34%).

We observe excesses of mortality for symptoms, signs, and ill-defined conditions (ICD-IX: 780-799) in the GeA among females (+ 62%) and in the SoA for both gender (males + 63%; females + 126%), while in the NoA a defect of mortality among females (- 36%) is reported.

It should be noticed that most of the previously commented results are significant for the age class > 65 years. Some results are significant for the age class 35-64, such as:

- diseases of the digestive system among males in the SoA;
- chronic liver diseases and cirrhosis among females of the GeA and for both gender of the SoA;
- injury and poisoning among males in the SoA.

Table 1
Standardized Mortality Ratios (SMRs) for each cause (or group of causes) of death, differentiated by area, gender and adjusted by deprivation index. Period 2003-2012

Disease	ICD-IX Code	GEOTHERMAL AREA				NORTHERN AREA				SOUTHERN AREA			
		MALES		FEMALES		MALES		FEMALES		MALES		FEMALES	
		OBS	SMR (CI 95%)	OBS	SMR (CI 95%)	OBS	SMR (CI 95%)	OBS	SMR (CI 95%)	OBS	SMR (CI 95%)	OBS	SMR (CI 95%)
All causes	0-999	3111	103 (100-107)	3330	101 (98-105)	1188	96 (90-101)	1256	98 (92-103)	1923	109 (104-114)	2074	104 (99-108)
Infectious and parasitic diseases	001-139	31	130 (88-185)	25	88 (57-130)	11	113 (56-202)	10	90 (43-166)	20	142 (87-220)	15	86 (48-143)
Tubercolosis	010-018	3	207 (42-605)		< 3		< 3		< 3		< 3		0
Viral hepatitis	070	5	122 (39-285)	4	81 (22-208)		< 3	3	156 (31-456)	4	164 (44-420)		< 3
Neoplasms	140-239	1015	104 (97-110)	712	97 (90-105)	342	86 (77-95)	258	91 (80-103)	673	116 (107-125)	454	102 (92-111)
Malignant neoplasm of lip, oral cavity, and pharynx	140-149	25	145 (94-214)	5	65 (21-153)	8	115 (50-228)	3	101 (20-296)	17	165 (96-263)		< 3
Malignant neoplasm of esophagus	150	13	95 (50-162)	6	132 (48-287)	4	72 (19-185)		< 3	9	110 (50-209)	5	179 (58-418)
Malignant neoplasm of stomach	151	94	118 (95-144)	68	117 (91-148)	25	77 (50-113)	22	97 (61-147)	69	146 (114-185)	46	129 (95-173)
Malignant neoplasm of colon and rectum	153-154	135	105 (88-125)	109	94 (78-114)	43	82 (60-111)	45	100 (73-134)	92	121 (98-149)	64	91 (70-116)
Malignant neoplasm of liver, gallbladder and bile ducts	155-156	76	124 (98-155)	53	113 (85-148)	20	81 (49-124)	21	115 (71-176)	56	153 (116-199)	32	112 (76-157)
Malignant neoplasm of pancreas	157	46	99 (72-132)	54	104 (78-136)	18	96 (57-151)	17	84 (49-135)	28	101 (67-147)	37	117 (82-161)
Malignant neoplasm of larynx	161	21	137 (85-210)		0	10	162 (77-298)		0	11	121 (60-216)		0
Malignant neoplasm of trachea, bronchus, and lung	162	234	98 (86-112)	55	82 (62-107)	69	72 (56-91)	16	62 (35-100)	165	117 (100-136)	39	95 (68-130)
Malignant neoplasm of pleura	163	9	134 (61-254)		< 3	6	220 (80-479)		< 3	3	75 (15-219)		0
Malignant neoplasm of connective and other sort of tissue	171		< 3		< 3		0		< 3		< 3	5	260 (84-608)
Malignant neoplasm of skin	172	9	82 (38-156)	7	89 (36-183)	4	91 (25-234)	3	99 (20-288)	5	76 (25-178)	4	82 (22-211)
Malignant neoplasm of breast	174-175		0	76	77 (61-97)		0	30	79 (53-112)		0	46	76 (56-102)
Malignant neoplasm of uterus	179-180, 182		0	23	81 (52-122)		0	11	101 (50-180)		0	12	69 (36-121)
Malignant neoplasm of ovary and other uterine adnexa	183		0	48	138 (102-183)		0	22	164 (103-248)		0	26	122 (80-179)
Malignant neoplasm of prostate	185	90	105 (85-129)		0	30	85 (57-121)		0	60	120 (91-154)		0
Malignant neoplasm of bladder	188	54	105 (79-136)	15	108 (60-178)	20	94 (58-146)	6	110 (40-240)	34	112 (77-156)	9	107 (49-202)
Malignant neoplasm of kidney and other and unspecified urinary organs	189	27	101 (67-147)	12	69 (35-120)	14	130 (71-217)		< 3	13	82 (44-140)	10	94 (45-172)
Malignant neoplasm of the central nervous system	191-192, 225, 239.6	29	104 (69-149)	38	148 (104-203)	10	89 (43-164)	9	91 (41-172)	19	114 (68-178)	29	184 (123-264)
Malignant neoplasm of lymphatic and hematopoietic tissue	200-208	62	81 (62-104)	64	94 (73-121)	31	100 (68-142)	27	103 (68-149)	31	69 (47-97)	37	89 (63-123)
Non Hodgkin lymphoma	200-202	19	78 (47-122)	18	83 (49-131)	10	101 (49-186)	8	95 (41-187)	9	62 (28-118)	10	76 (36-139)
Hodgkin's disease	201		< 3		< 3		< 3		< 3		0		0

Continues

Table 1
Continues

Disease	ICD-IX Code	GEOTHERMAL AREA				NORTHERN AREA				SOUTHERN AREA			
		MALES		FEMALES		MALES		FEMALES		MALES		FEMALES	
		OBS	SMR (CI 95%)	OBS	SMR (CI 95%)	OBS	SMR (CI 95%)	OBS	SMR (CI 95%)	OBS	SMR (CI 95%)	OBS	SMR (CI 95%)
Multiple myeloma	203	19	105 (63-163)	16	94 (53-152)	8	108 (46-212)	4	60 (16-154)	11	103 (51-183)	12	115 (59-200)
Leukemia	204-208	23	73 (46-110)	28	103 (69-149)	12	94 (48-164)	13	123 (66-211)	11	59 (29-106)	15	91 (51-149)
Diabetes mellitus	250	76	100 (79-125)	102	93 (76-113)	28	89 (59-129)	35	81 (57-113)	48	107 (79-142)	67	101 (78-128)
Senile and presenile organic psychotic conditions	290	22	66 (42-100)	90	108 (87-132)	8	57 (25-112)	44	134 (97-179)	14	73 (40-122)	46	91 (66-121)
Diseases of the nervous system and sense organs	320-389	96	96 (78-117)	134	94 (79-112)	44	107 (78-143)	54	97 (73-126)	52	88 (66-116)	80	93 (73-115)
Parkinson's disease	332	37	135 (95-186)	26	98 (64-144)	14	123 (67-207)	10	96 (46-177)	23	144 (91-216)	16	99 (57-162)
Motor neuron disease	335.2	7	96 (39-198)	8	107 (46-211)		< 3	4	139 (37-356)	6	138 (50-299)	4	87 (23-224)
Multiple sclerosis	340		< 3		0		< 3		0		0		0
Epilepsy	345		< 3		< 3		0		< 3		< 3		< 3
Diseases of the circulatory system	390-459	1067	95 (89-101)	1471	97 (92-102)	467	100 (91-110)	611	102 (94-110)	600	91 (84-99)	860	93 (87-99)
Hypertensive disease	401-405	51	92 (69-121)	114	103 (85-124)	22	96 (60-145)	52	120 (89-157)	29	90 (60-129)	62	92 (71-118)
Acute myocardial infarction of anterolateral wall	410	141	86 (72-101)	148	99 (84-117)	60	89 (68-115)	64	109 (84-140)	81	83 (66-104)	84	93 (74-115)
Ischemic heart disease	410-414	338	86 (77-96)	325	81 (73-91)	157	97 (83-114)	141	90 (76-106)	181	79 (68-91)	184	76 (65-88)
Cerebrovascular disease	430-438	313	99 (88-110)	501	104 (95-113)	143	109 (91-128)	219	115 (101-132)	170	92 (79-107)	282	96 (85-108)
Diseases of the respiratory system	460-519	348	134 (120-149)	199	110 (95-127)	143	132 (111-155)	72	102 (79-128)	205	135 (117-155)	127	116 (97-138)
Acute respiratory infections	460-466, 480-487	63	110 (84-141)	74	121 (95-151)	19	79 (48-124)	21	87 (54-133)	44	132 (96-177)	53	142 (107-186)
Pneumonia	480-486	60	113 (86-146)	61	115 (88-148)	19	86 (52-134)	17	82 (48-131)	41	133 (95-180)	44	137 (100-184)
Bronchopneumopathy chronic obstructive	491-492, 494-496	153	119 (101-139)	76	108 (85-135)	66	123 (95-156)	33	120 (82-168)	87	116 (93-143)	43	101 (73-136)
Asthma	493	2	109 (12-395)	8	167 (72-330)		< 3	3	161 (32-470)		< 3	5	172 (55-400)
Pneumoconiosis	500-505	79	325 (258-406)		0 (0-4745)	37	364 (256-502)		0	42	298 (215-402)		0
Diseases of the digestive system	520-579	123	110 (91-131)	171	134 (114-155)	39	85 (61-117)	57	114 (86-148)	84	127 (101-157)	114	147 (121-176)
Chronic liver disease and cirrhosis	571	44	125 (91-168)	43	148 (107-199)	10	71 (34-131)	13	115 (61-197)	34	161 (111-224)	30	169 (114-241)
Diseases of the genitourinary system	580-629	55	94 (70-122)	66	105 (81-133)	24	98 (63-146)	32	130 (89-183)	31	90 (61-128)	34	89 (61-124)
Nephritis	581-583		0		< 3		0		< 3		0		0
Acute and chronic renal failure	584-585	53	112 (84-147)	55	105 (79-137)	22	112 (70-169)	24	117 (75-175)	31	112 (76-159)	31	98 (66-139)
Congenital anomalies	740-759	7	180 (72-370)	8	199 (86-392)		< 3		< 3	6	256 (93-556)	6	243 (89-529)
Symptoms, signs, and ill-defined conditions	780-799	49	122 (90-161)	155	162 (137-189)	11	65 (32-116)	24	64 (41-95)	38	163 (115-224)	131	226 (189-268)
Injury and poisoning	800-999	157	116 (99-136)	96	104 (85-128)	49	90 (67-119)	31	86 (59-123)	108	134 (110-162)	65	116 (90-148)

Legend: OBS: observed; SMR: Standardized Mortality Ratio; CI 95%: Confidence Interval for 95th Percentile.
Note: Statistically significant excesses of mortality are highlighted in orange. Statistically significant defects of mortality are highlighted in green. Results approaching but not reaching statistical significance are highlighted in blue.

DISCUSSION

Between 2003 and 2012, an excess of mortality for all causes approaching but not reaching statistical significance is observed among males in the GeA of Tuscany, confirming previous results. In this study mortality in excess among males is relevant for diseases of the respiratory system, in particular for pneumoconiosis, as in the preceding study, and for bronchopneumopathy chronic obstructive. Compared to the previous study [14], excesses of mortality for infectious and parasitic diseases, tuberculosis, diseases of the nervous system among males of GeA are not confirmed (*Table 2*). In fact, these causes have a multifactorial etiology. For instance, pneumoconiosis is associated with occupational exposures [19-27], and is one of the most important risk factors for pulmonary tuberculosis [28-32]. Usually, going forward in time, mortality due to work activities (mining, in this case) decreases. In this framework, to explain the fact that past results are not confirmed, the gradual extinction since the 80s of the cohorts of workers employed in mining activities seems to be likely. Regarding females, excesses of mortality for cancer of the ovary and other uterine adnexa, of the central nervous system and digestive system diseases, and a lower mortality for breast cancer are observed. Furthermore, compared to the previous study, excesses of mortality for liver diseases and cirrhosis and lower mortality for circulatory system diseases and ischemic heart diseases are confirmed (*Table 2*). High mortality from cirrhosis focuses attention towards the exposure to hepatitis B and C, or long-term alcohol abuse, rather than towards factors of environmental pollution [33]. Lower mortality for ischemic heart disease observed in both gender is not easy to interpret due to many recognized risk factors [34].

A clear geographical heterogeneity appears, with a mortality profile worst in the south than in the north, as previously observed.

In fact, in the NoA, mortality among males from cancers of all sites and in particular for lung cancer is lower than expected, and only mortality for diseases of the respiratory system, particularly for pneumoconiosis, is reported in excess. Among females, significant excesses for ovarian cancer and cerebrovascular diseases are reported, confirming previous results (*Table 2*). Several risk factors, including exposure to asbestos, are recognized associated with ovarian cancer [34, 35]. For cerebrovascular diseases there is sufficient evidence for environmental factors, smoking habit and alcohol consumption [36]. Our results are in agreement with literature [6, 10] only with regard to respiratory system diseases among men, not among women. At the same time, we do not detect excesses of neurological causes observed in other studies [6, 7]. In summary, in the NoA, where the majority of geothermal power plants are located, few excesses of mortality emerge. Some of these are reasonably attributable to occupational factors, as for pneumoconiosis among males. Other excesses are instead potentially associated with multiple risk factors, as for cerebrovascular diseases among females.

Among males in the SoA, total mortality, mortality for all cancers, particularly liver cancer, exceeds the expectation confirming previous results. This study identifies an excess of mortality for stomach cancer not observed before and an excess approaching but not reaching statistical significance for lung cancer confirming previous findings (*Table 2*).

In this regard it is noteworthy that a high incidence of stomach cancer has been reported for a long time in several mountain areas of Tuscany. Although major epidemiological evidence of the causes of stomach cancer is attributable to cigarettes smoking, socioeconomic factors, diet, exposure to *Helicobacter pylori*, and genetic factors [36], the role of environmental factors, in particular exposure to chemical contaminants, cannot be excluded [37]. The occurrence of liver cancer is instead related to chronic damage of the liver and its determinants, including alcohol abuse and infections from hepatitis B and C viruses [38-41]. Excesses of mortality among males for diseases of the respiratory system, particularly for pneumoconiosis are observed as in the previous study. This study reveals excesses of mortality for the digestive system, particularly for cirrhosis and defects for cancer of lymphatic and hematopoietic tissue and for circulatory system diseases, in particular for ischemic heart disease not observed before (*Table 2*). Since the significant excess of mortality for diseases of the respiratory system in the SoA is observed only among males, past occupational exposures and tobacco smoking habit are the more reasonably plausible causes.

Among females of the SoA excesses of mortality for cancer of the central nervous system, for pneumonia and cirrhosis are observed and excesses of mortality for acute respiratory infections, particularly pneumoconiosis, and for digestive system diseases are confirmed (*Table 2*).

Significant defect of mortality for circulatory system diseases, particularly for ischemic heart disease, is also observed among females of the SoA, as it occurs among males.

In an area with emissions from geothermal plants, mortality excesses of diseases with a short incubation period, as for acute respiratory diseases, for which it is difficult to assign a role of occupational exposures, a targeted strategy of environmental monitoring and epidemiological surveillance seems appropriate.

It should be noted that among acute respiratory diseases, pneumonia seems to be the most common, in particular in the age class ≥ 65 years. This is often of questionable reliability in death certificates.

The mortality excess for digestive system diseases is largely attributable to liver cirrhosis in the SoA. It is complex to interpret a lower mortality from cerebrovascular diseases only among females.

In summary, this study shows a worst mortality profile in the SoA, especially in males, for whom excesses for all cancers and some causes of cancer emerge, while in the NoA an excess for cerebrovascular diseases among females is noteworthy.

Finally, although the role of ecological (or geographical) studies in epidemiology and their consequences in public health have been addressed in several scientific papers [42-45], it should be reminded that this kind of study, adopted in this work, is not suitable for produc-

Table 2

Standardized Mortality Ratios (SMRs) for each cause (or group of causes) of death, differentiated by area, gender, period of analysis (2000-2006; 2003-2013) and adjusted by deprivation index

Disease	GEOTHERMAL AREA				NORTHERN AREA				SOUTHERN AREA			
	MALES SMR (CI 95%)		FEMALES SMR (CI 95%)		MALES SMR (CI 95%)		FEMALES SMR (CI 95%)		MALES SMR (CI 95%)		FEMALES SMR (CI 95%)	
	2000-2006	2003-2012	2000-2006	2003-2012	2000-2006	2003-2012	2000-2006	2003-2012	2000-2006	2003-2012	2000-2006	2003-2012
All causes	108 (103-112)	103 (100-107)							115 (109-211)	109 (104-114)		
Infectious and parasitic diseases	245 (159-362)	130 (88-185)			250 (125-447)	113 (56-202)						
Tubercolosis	421 (182-830)	207 (42-605)							539 (216-1109)	*		
Neoplasms					87 (76-98)	86 (77-95)			121 (110-131)	116 (107-125)		
Malignant neoplasm of stomach									122 (91-159)	146 (114-185)		
Malignant neoplasm of liver, gallbladder and bile ducts									171 (122-234)	153 (116-199)		
Malignant neoplasm of trachea, bronchus, and lung					78 (59-101)	72 (56-91)			121 (101-145)	117 (100-136)		
Malignant neoplasm of breast			80 (60-104)	77 (61-97)								
Malignant neoplasm of ovary and other uterine adnexa			126 (84-181)	138 (102-183)			172 (100-275)	164 (103-248)				
Malignant neoplasm of the central nervous system			108 (68-164)	148 (104-203)							109 (60-184)	184 (123-264)
Malignant neoplasm of lymphatic and hematopoietic tissue									101 (68-144)	69 (47-97)		
Diseases of the nervous system and sense organs	130 (101-163)	96 (78-117)										
Diseases of the circulatory system			96 (91-102)	97 (92-102)					103 (94-113)	91 (84-99)	94 (87-102)	93 (87-99)
Ischemic heart disease			85 (74-97)	81 (73-91)					101 (86-118)	79 (68-91)	87 (73-104)	76 (65-88)
Cerebrovascular disease							122 (104-142)	115 (101-132)				
Diseases of the respiratory system	129 (112-147)	134 (120-149)			124 (99-152)	132 (111-155)			132 (110-157)	135 (117-155)		
Acute respiratory infections											142 (102-193)	142 (107-186)
Pneumonia											120 (81-173)	137 (100-184)
Bronchopneumopathy chronic obstructive		119 (101-139)										
Pneumoconiosis	372 (277-489)	325 (258-406)			351 (214-542)	364 (256-502)			388 (263-550)	298 (215-402)		
Diseases of the digestive system			117 (96-142)	134 (114-155)					125 (95-162)	127 (101-157)	130 (102-164)	147 (121-176)
Chronic liver disease and cirrhosis			143 (100-199)	148 (107-199)					151 (99-219)	161 (111-224)	153 (97-230)	169 (114-241)
Symptoms, signs, and ill-defined conditions			147 (113-187)	162 (137-189)			61 (29-111)	64 (41-95)	190 (119-287)	163 (115-224)	197 (148-255)	226 (189-268)
Injury and poisoning									119 (94-149)	134 (110-162)	134 (101-173)	116 (90-148)

Legend: SMR: Standardized Mortality Ratio; CI: Confidence Interval. *SMR is not reported because the number of observations is less than 3.
Note: Statistically significant excesses of mortality are highlighted in orange. Statistically significant defects of mortality are highlighted in green. Results approaching but not reaching statistical significance are highlighted in blue.

ing evidence on the cause-effect relationship. The major limitation of this design is the assumption of the residence at municipal level as a valid measure of exposure to both environmental and socio-economic factors. In fact, using aggregated health data can lead to results affected by ecological fallacy [44, 46, 47]. Despite these limitations, well conducted ecological studies can show a satisfying scientific standard, also requiring a careful integrated reading of their results over time and space and specific for each disease [48, 49]. Furthermore, such results can be integrated with studies on the strength of environment-health associations, using individual-level data, able to provide a precise spatio-temporal characterization [50-52]. On the other hand, the study with macro-aggregated data (*e.g.* municipality level) is well recognized to be a useful first step to proceed towards studies with more advanced design for the understanding of the causal relationship [51, 53-56].

CONCLUSIONS

Taking into account limitations of studies with descriptive epidemiological design, solely based on aggregated environmental and health data, analyses performed in this study show an epidemiological picture of the GeA similar to the one of adjacent not geothermal municipalities. However, there is no lack of critical elements related to certain levels of environmental pollution and to mortality excesses observed for a limited number of diseases, most evident in the SoA than in the NoA. Overall results, most critical for males, suggest that the major determinants of weaknesses observed in health profile are to be found mainly in occupations associated with productive activities of the past, without excluding recent exposures related to individual lifestyles, environmental agents or other factors not currently known. To clarify the etiology of acute respiratory diseases, in excess among women of the SoA, and cerebrovascular diseases, in excess among women of the NoA, analytical studies seem to be appropriate.

Although the study design does not allow us any speculation about the cause-effect relationship, the observed mortality excesses in areas with documented presence of pollution and with high concern of local communities have strengthened directions for environmental improvement and monitoring, and have suggested priority settings for further environmental epidemiology insights to the regional and local authorities. A program including targeted etiological studies and human biomonitoring surveys is under development by the Regional government of Tuscany [57].

Author's contribution statement

Elisa Bustaffa drafted the manuscript and interpreted the results. All Authors conceived and designed the study.

Elisa Bustaffa, Fabrizio Minichilli and Daniela Nuvolone contributed to data acquisition and performed statistical analyses. Daniela Nuvolone and Fabio Voller revised the manuscript. Fabrizio Bianchi and Francesco Cipriani revised the manuscript for important critical content.

Conflict of interest statement

Authors certify that they have no affiliations with or involvement in any organization or entity with any financial interest, or non-financial interest in the subject matter or materials discussed in this manuscript.

Received on 7 December 2016.
Accepted on 23 January 2017.

REFERENCES

1. Barbier E, Santoprete G. *L'energia geotermica. Una fonte di energia all'interno della terra*. Torino: Giappichelli Editore; 1993.
2. Dickson MH, Fanelli M. *Geothermal energy utilization and technology*. London: Earthscan; 2003.
3. ARPAT. *Monitoraggio aree geotermiche*. Firenze: ARPAT; 2002.
4. Bates MN, Garrett N, Graham B, Read D. Air pollution and mortality in the Rotorua geothermal area. *Aust N Z J Public Health* 1997;21:581-6.
5. Bates MN, Garrett N, Graham B, Read D. Cancer incidence, morbidity and geothermal air pollution in Rotorua. New Zealand. *Int J Epidemiol* 1998;27:10-4.
6. Bates MN, Garrett N, Shoemack P. Investigation of health effects of hydrogen sulfide from a geothermal source. *Arch Environ Health* 2002;57:405-11.
7. Legator MS, Singleton CR, Morris DL, Philips DL. Health effects from chronic low-level exposure to hydrogen sulfide. *Arch Environ Health* 2001;56:123-31.
8. World Health Organization. Air quality guidelines for Europe; 2 ed. *WHO regional publications* 2000;91:146-8.
9. World Health Organization. *Concise international chemical assessment document 53 hydrogen sulfide: human health aspects*. Geneva: WHO; 2003.
10. Durand M, Wilson JG. Spatial analysis of respiratory disease on an urbanized geothermal field. *Environ Res* 2006;101:238-45. DOI: 10.1016-j.envres.2005.08.006.
11. Bates MN, Garrett N, Crane J, Balmes JR. Associations of ambient hydrogen sulfide exposure with self-reported asthma and asthma symptoms. *Environ Res* 2013;122:81-7. DOI: 10.1016/j.envres.2013.02.002
12. Reed BR, Crane J, Garret N, Woods DL, Bates MN. Chronic ambient hydrogen sulfide exposure and cognitive function. *Neurotoxicol and Teratol* 2014;42:68-76. DOI: 10.1016/j.ntt.2014.02.002
13. Bates MN, Crane J, Balmes JR, Garrett N. Investigation of hydrogen sulfide exposure and lung function, asthma and chronic obstructive pulmonary disease in a geothermal area of New Zealand. *PLos ONE* 2015;10(3):e0122062. DOI: 10.1371/journal.pone.0122062.
14. Minichilli F, Nuvolone D, Bustaffa E, Cipriani F, Vigotti MA, Bianchi F. State of health of populations residing in geothermal areas of Tuscany. *Epidemiol Prev* 2012;36(5 Suppl. 1):1-104.
15. Agenzia Regionale Protezione Ambiente Toscana. Monitoraggio *delle aree geotermiche – Rapporto finale biennio 2007-2008*. Firenze: ARPAT; 2009. Available from: www.arpat.toscana.it/progetti/geotermia
16. Agenzia regionale per la protezione ambientale della Toscana. *Monitoraggio delle aree geotermiche toscane. Concen-*

trazioni di idrogeno solforato nelle aree geotermiche toscane. Validazione dati ENEL e monitoraggi ARPAT. Firenze: ARPAT; 2014.
17. Breslow NE, Day NE. *Statistical methods in cancer research. Volume II: The design and analysis of cohort studies.* Oxford-New York: Oxford University Press; 1987. (IARC Scientific Publications Mo. 82).
18. Caranci N, Biggeri A, Grisotto L, Pacelli B, Spadea T, Costa G. The Italian deprivation index at census block level: definition, description and association with general mortality. *Epidemiol Prev* 2010;34(4):167-76.
19. Carta P, Aru G, Manca P. Mortality for lung cancer among silicotic patients in Sardinia: an update study with 10 more years of follow up. *Occup Environ Med* 2001;58:786-93.
20. Puntoni R, Merlo F, Borsa L, Reggiardo G, Garrone E, Ceppi M. A historical cohort mortality study among shipyard workers in Genoa, Italy. *Am J Ind Med* 2001;40(4):363-70.
21. Glazer CS, Newmann LS. Occupational interstitial lung disease. *Clin Chest Med* 2004;25:467-78.
22. Antão VC, Pinheiro GA, Parker JE. Lung disease associated with silicates and other dusts. In: Rom WN, Markovitz S (Eds). *Environmental and occupational medicine*. 4th ed. Philadelphia: Lippincott Williams & Wilkins; 2007.
23. Attfield MD, Castranova V, Wagner GR. Respiratory disease in coal miners. In: Rom WN, Markovitz S (Eds). *Environmental and occupational medicine*. 4th ed. Philadelphia: Lippincott Williams & Wilkins; 2007.
24. Jalloul AS, Banks DE. The health effects of silica exposure. In: Rom WN, Markovitz S (Eds). *Environmental and occupational medicine*. 4th ed. Philadelphia: Lippincott Williams & Wilkins; 2007.
25. Madden EE, Fowler BA. Metal compounds and rare earths. In: Rom WN, Markovitz S (Eds). *Environmental and occupational medicine*. 4th ed. Philadelphia: Lippincott Williams & Wilkins; 2007.
26. Raffaelli I, Festa G, Costantini AS, Leva G, Gorini G. Mortality in a color of asbestos workerws in Carrara, Italy. *Med Lav* 2007;98(2):156-63.
27. Rom WN. Asbestosis, pleural fibrosis, and lung cancer. In: Rom WN, Markovitz S (Eds). *Environmental and occupational medicine*. 4th ed. Philadelphia: Lippincott Williams & Wilkins; 2007.
28. ATS/CDC Statement Committee on Latent Tubercolosis Infection. Targeted tuberculin testing and treatment of latent tubercolosis infection. American Thoracic Society. *MMWR Recomm Rep* 2000;49(RR-6):1-51.
29. World Health Organization. *Global tubercolosis control-surveillance, planning, financing*. WHO Report; 2006.
30. Davies PD, Yew WW, Ganguly D, Davidow AL, Reichman LB, Dheda K, Rook GA. Smoking and tubercolosis: the epidemiological association and immunopathogenesis. *Trans R Soc Trop Med Hyg* 2006;100(4):291-8.
31. Restrepo BI. Convergence of the tubercolosis and diabetes epidemics: renewal of old acquaintances. *Clin Infect Dis* 2007;45(4):436-8.
32. Chaisson RE, Martinson NA. Tubercolosis in Africa – combating an HIV-driven crisis. *N Engl J Med* 2008;358(11):1089-92.
33. Johnson D, Groopman JD. Toxic liver disorders. In: Rom WN, Markovitz S (Eds). *Environmental and occupational medicine*. 4th ed. Philadelphia: Lippincott Williams & Wilkins; 2007.
34. Pirastu R, Ancona C, Iavarone I, Mitis F, Zona A, Comba P, SENTIERI Working Group, SENTIERI Project. Mortality study of residents in Italian polpute sites: evaluation of the epidemiological evidence. *Epidemiol Prev* 2010;34(5-6 Suppl.):1-2.
35. Reid A, Heyworth J, de Klerk NH, Musk B. Cancer incidence among women and girls environmentally and occupationally exposed to blue asbestos at Wittenoom, Western Australia. *Int J Cancer* 2008;122(10):2337-44.
36. Reid A, Berry G, Heyworth J, de Klerk NH, Musk AW. Predicted mortality from malignant mesothelioma among women exposed to blue asbestos at Wittenoom, Western Australia. *Occup Environ Med* 2009;66(3):169-74. DOI: 10.1136/oem.2077.038315
37. Clapp RW, Howe GK, Jacobs MM. Environmental and occupational causes of cancer. A review of recent scientific literature. *Biomed Pharmacother* 2007;61(10):631-9. DOI: 10.1016/j.biopha.2007.08.001
38. Room B, Babor T, Rehm J. Alcohol and public health. *Lancet* 2005;365:519-30.
39. Boffetta P, Hashibe M. Alcohol and cancer. *Lancet Oncol* 2006;7:149-56.
40. London WT, McGlynn KA. Liver cancer. In: Scottenfeld D, Fraumeni JF Jr (Eds). *Cancer Epidemiology and Prevention*. 3rd ed. New York: Oxford University Press; 2006.
41. Baan R, Straif K, Grosse Y, Secretan B, E Ghissassi F, Bouvard V, Altieri A, Cogliano V, WHO International Agency for Research on Cancer Monograph Working Group. Carcinogenicity of alcoholic beverages. *Lancet Oncol* 2007;8(4):292-3.
42. Cislaghi C, Luppi G, Biggeri A, Braga M, Terracini B. Le analisi spaziali in Epidemiologia. *Epidemiol Prev* 1995;19:131-228.
43. Elliot P, Martuzzi M, Shaddick G. Spatial statistical methods in environmental epidemiology: a critique. *Stat Methods Med Res* 1995;4(2):137-59.
44. Elliott P, Wakefield JC, Best NG, Briggs DJ. *Spatial epidemiology, methods and applications*. Oxford: Oxford University Press; 2000.
45. Martuzzi M, Mitis F, Biggeri A, Terracini B, Bertollini R. Ambiente e stato di salute nella popolazione delle aree ad alto rischio di crisi ambientale in Italia. *Epidemiol Prev* 2002;26(6):1-56.
46. Morgenstern H. *Ecologic studies in Rothman KJ and Greenland S. Modern Epidemiology*. Philadelphia: Lippincott-Raven Publishers; 1998.
47. Last JM. *A Dictionary of Public Health*. Oxford-New York: Oxford University Press; 2007.
48. Terracini B. Inquadramento teorico e metodologico. In: Cori L, Cocchi M, Comba P. *Indagini epidemiologiche nei siti di interesse nazionale per le bonifiche delle regioni Ob. 1 dell'Unione Europea*. Roma: Istituto Superiore di Sanità; 2005. (Rapporti ISTISAN, 05/1).
49. Terracini B. Il ruolo dell'epidemiologia nella valutazione dell'impatto di salute nei siti inquinati. In: Comba P, Bianchi F, Iavarone I, Pirastu R (Ed). *Impatto sulla salute dei siti inquinati: metodi e strumenti per la ricerca e le valutazioni*. Roma: Istituto Superiore di Sanità; 2007. (Rapporti ISTISAN, 07/50).
50. Schwartz M. The fallacy of ecological fallacy: the potential misuse of a concept and consequences. *Am J Public Health* 1994;84:819-23.
51. Susser M. The logic in ecological: II. The logic of design. *Am J Pubic Health* 1994;84:830-5.
52. Pearce N. The rise of corporate epidemiology and the narrowing of epidemiology's vision. *Int J Epidemiol* 2007;36(4):713-7. DOI:10.1093/ije/dym152
53. Susser M. Does risk factor epidemiology put epidemiology at risk? Peering into the future. *J Epidemiol Community Health* 1998;52(10):608-11.
54. Pearce N. Traditional epidemiology, modern epidemiology, and public health. *Am J Public Health* 1996;86(5):678-83.

55. Pearce N. The ecological fallacy strikes back. *J Epidemiol Community Health* 2000;54:326-7.
56. Susser M, Susser E. Choosing a future for epidemiology: I. Eras and paradigms. *Am J Public Health* 1996;86(5):668-73.
57. ARS Toscana. *Geotermia e salute in Toscana. Quarta fase della ricerca epidemiologica dell'area geotermica toscana*. Available from: https://ars.toscana.it/it/geotermia-e-salute/quarta-fase-della-ricerca-epidemiologica-dellarea-geotermica-toscana.