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Cancer mortality trends between 1988 and 2009 in the metropolitan area of Naples and Caserta, Southern Italy

Results from a joinpoint regression analysis

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Mortality data by geographic area and trend-based surveillance are particularly relevant in orienting public health decisions targeting specific populations. We analyzed overall and site-specific cancer mortality between 1988 and 2009 in the metropolitan area of Naples and Caserta in southern Italy. Age-standardized mortality rates (SMR) were computed for each 5-y age group, by gender, primitive cancer site and specific Province in the overall population and age-defined subgroups. Cancer mortality trends were quantified by annual percent change (APC) and 95% confidence interval (CI). From Naples and Caserta, the reduction observed between 1988 and 2009 in SMR in males, but not in females, was significantly lower compared with the decrease reported at a national level (–11.4% and –28.4%, respectively). In elderly men, differences between local and national SMR were more pronounced (+13.6% compared with –2.7%). In males, the joinpoint regression analysis showed the following APC and 95% CI: –0.9%/year (–1.2; –0.7) and –0.6%/year (–1.0; –0.2) for Naples and Caserta, respectively. In females, estimates were –0.6%/year (–0.8; –0.5) and –0.7%/year (–1.2; –0.3). The overall orientation toward declining cancer mortality trends appeared in antithesis with the slight, but significant, increase for some tumors (e.g., pancreatic cancer in both genders). A complex mixture of heterogeneous factors concurs to explain the evidence observed including lifestyle, access to screening procedures, advancements in cancer diagnosis and treatment. Further details might eventually derive from biomonitoring studies for ascertaining the causal link between exposure to potential contaminants in air, water, and soil and cancer-related outcomes in the area of interest.

Introduction

Cancer mortality data, along with cancer incidence and population based survival, are a cornerstone of epidemiology research, health monitoring and resource allocation for interventions aimed at cancer prevention and control. In recent years, a number of reports on cancer mortality trends have been published in Italy and other countries. Consistent with other European countries and the United States, Italy has shown declining trends in overall cancer mortality since the end of the 20th century, with mortality rates decreasing by 1.8 percent (%) and 1.1% yearly in men and women, respectively.[1,2]

Data availability by geographic area might render trend-based surveillance particularly relevant in public health decision making for specific target populations. Historically, in Italy, the comparison of mortality and morbidity indicators by broad geographical areas has highlighted discrepancies, with southern Italy having a lower cancer burden compared with the north and center.[3,4] However, recent evidence suggests that southern Italy is progressively losing its advantage in mortality from cancer.[5-8] Moreover, recent data from a geographical study have shown significant cancer mortality excess in 7 out of 23 southern provinces, with the highest standardized mortality rates in the provinces of Naples and Caserta.[9] These two provinces converge in a metropolitan area whose distinctive features are the high population density (9.026 person/km^2), one of the highest in Europe, and widespread industrialization process and related activities.[10]

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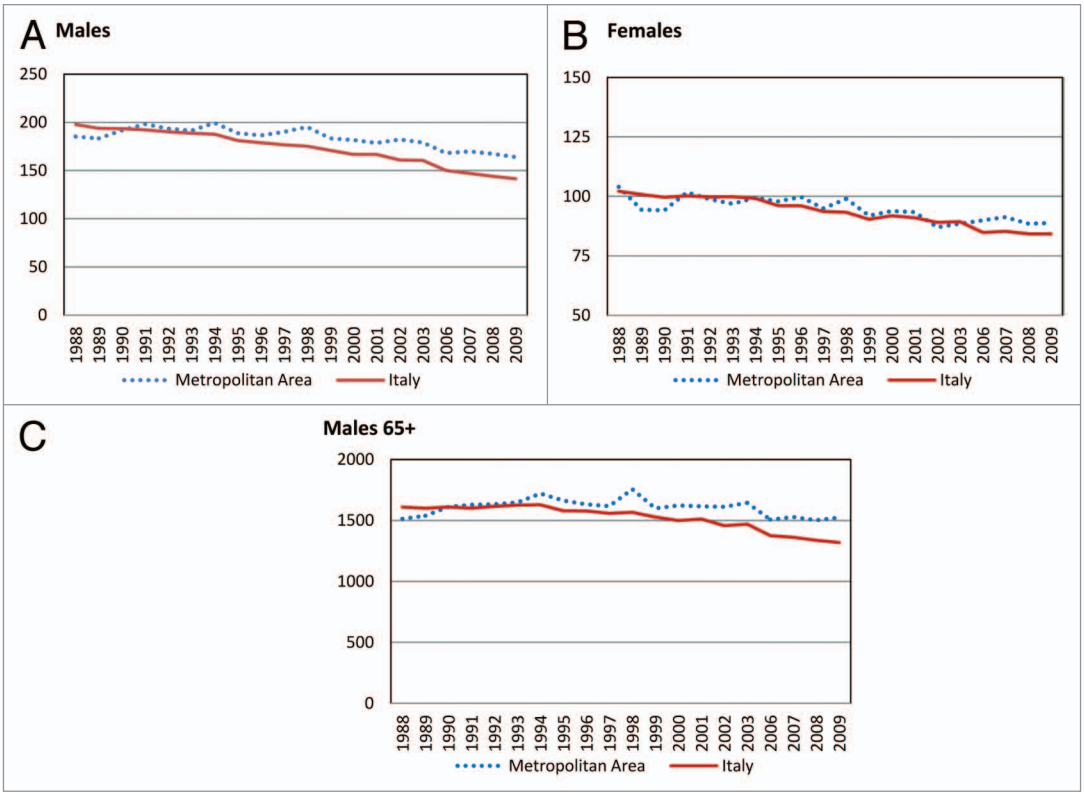

Figure 1. (**A and B**) Word standardized mortality rates × 100 000 inhabitants (dotted line, metropolitan area; solid line, Italy) from 1988 to 2009 for all cancer site by gender. (**C**) Word standardized mortality rates × 100 000 inhabitants in males aged 65 and older (dotted line, metropolitan area; solid line, Italy) from 1988 to 2009 for all cancer sites.

In the present study, we aimed to analyze overall and site-specific cancer mortality between 1988 and 2009 in the metropolitan area of Naples and Caserta, southern Italy. Cancer mortality related to the area of interest was also presented in a frame including cancer estimates from Italy overall. The independent effect of aging on the evolution of cancer mortality trends was evaluated in men and women aged 65 and older at the time of death. Potential explanatory factors for observed mortality trends were then discussed, along with the role of health service interventions.

Results

Between 1988 and 2009, the population of the metropolitan area of Naples and Caserta accounted for a total number of 3 912 068 inhabitants out of 5 701 931 over the entire Campania region. Certified deaths from the metropolitan area of interest during the whole study period were 94 010 and 63 995 for males and females, respectively (data available upon request).

Word standardized mortality rates (SMR) for the metropolitan area of Naples and Caserta and Italy overall between 1988 and 2009 appear in **Figure 1**. Estimates are reported by gender and referred to all ages. In males, SMR for the metropolitan area of interest decreased from 185.3/100 000 in 1988 to 164.1/100 000 in 2009, with an overall 11.4% reduction. The decrease in SMR was more evident at a national level, with rates dropping from 197.9/100 000 to 141.6/100 000, with an overall 28.4% reduction (**Fig. 1A**). Conversely, in females, the decrease in SMR observed for the metropolitan area of Naples and Caserta did not substantially differ from the same estimates for Italy overall (**Fig. 1B**).

When confining the analysis to men aged 65 y and older, percent variations in standardized mortality for Naples and Caserta tended to diverge from those for Italy overall. We observed a gradual and steady decline in the national SMR from 1609.7/100 000 in 1988 to 1319.2/100 000 in 2009, with an overall 18.05% decrease. Conversely, standardized mortality for the metropolitan area of Naples and Caserta showed a 0.7% increase, with cancer deaths rising from 1513.6/100 000 in 1988 to 1524.6/100 000 in 2009 (**Fig. 1C**). In an additional analysis conducted in this same subgroup (i.e., males aged 65 and older) and restricted to the time frame between 2006 and 2009, the differences in mortality emerged more clearly, with national estimates decreasing from 1372 to 1319.1 (i.e., 3.8% decrease) and estimates for the metropolitan area increasing from 1507.6 to 1524. (i.e., 1.2% increase) (**Fig. 2**).

For women aged 65 y and older, there was a substantial overlap in SMR for the metropolitan area and Italy overall, both in the 1988–2009 time frame and between 2006 and 2009 (**Fig. S1**).

Results from the joinpoint regression analysis are shown in **Tables 1 and 2**. Estimated annual percent changes (APC) and related 95% confidence intervals (CI) are given by gender and cancer site relatively to each of the two provinces converging in

the metropolitan area and referred to the time frame spanning from 1998 to 2009.

In males, the APC for all cancer sites declined slightly, though significantly, during the whole period 1988–2009 (–0.9%/year [–1.2; –0.7] and –0.6%/year [–1.0; –0.2] for Naples and Caserta, respectively). Significant reductions in APC were consistent across the two provinces for the following primitive cancer sites: esophagus (–2.9%/year [–4.1; –1.7] in Naples and –2.4%/year [–4.4; –0.2] in Caserta), stomach (–2.5%/year [–3.1; –1.8] and –2.0%/year [–2.8; –1.2]), lung (–1.4%/year [–1.7; –1.1) and –1.0%/year [–1.4; –0.5]), bladder (–2.8%/year [–3.3; –2.3]0 and –1.6%/year [–2.6; –0.6]) and brain (–4.2%/year [–6.1; –2.2] and –2.3%/year [–4.3; –0.3]). A significant increase in cancer mortality with positive APC was found regarding intestines (+0.9%/year [+0.1;+0.6]) in the province of Caserta and pancreas (+1.9%/year [+1.0;+2.9] and +1.7%/year [+0.06;+3.4]) in Naples and Caserta, respectively (**Table 1**). In females, cancer related mortality showed similar trends for all cancer sites across the two provinces, with APC of –0.6%/year [–0.8; –0.5) and –0.7%/year (–1.2; –0.3) in Naples and Caserta, respectively. A significant reduction in APC was observed in both provinces for the following cancer sites: stomach (–1.9%/year [–2.7; –1.0] in Naples and –2.3%/year [–3.5; –1.06] in Caserta), liver (–2.5%/year [–3.1; –1.8) and –2.7%/year [–4.1; –1.4]), and uterus (–3.6%/year [–4.4; –2.7] and –3.8%/year [–5.2; –2.4]). APC for deaths related to cancers originating from intestines, breast, bladder, and Hodgkin disease were significantly reduced in Naples only (–1.1%/year [–1.6; –0.6), –1.0%/year [–1.4; –0.6], –2.1%/year [–3.4; –0.8], and –3.4%/year [–5.8; –0.9], respectively). Significant increase in cancer mortality with positive APC was found for pancreas in both provinces (+2.0%/year [+1.2; +2.7] and +2.5%/year [+0.7; +4.4], for Naples and Caserta, respectively) and for non-Hodgkin lymphoma in Naples only (+2.0%/year [+0.2; +3.7]).

Results from a joinpoint analysis restricted to elderly people from the metropolitan area are shown in **Table 3**. In men, there was a suggestion for a decrease in mortality for all cancer sites, even though estimates did not reach the statistical significance (–0.3 [–0.6; 0.0]). In women, overall APC showed a slight, significant decrease (–0.4 [–0.6; –0.2]). Estimates by cancer site confirmed previous results, with significantly decreased APC for stomach and lung (–1.7 [–2.4; –0.9), and –0.4 [–0.7, –0.01], respectively) and increased APC for non-Hodgkin lymphoma in males (+1.4 [+0.3; +2.6]). In females, data confirmed decreased APC for intestines, liver, and breast (–1.0 [–1.5; –0.6], –1.6 [–2.2; –1.0], and –0.6 [–1.1; –0.08]), while an increased APC was confirmed for lung (+1.6 [+0.7; +2.5]). Mortality trends for pancreatic cancer showed a significant increase in both genders (+1.7 [+0.9; +2.5] and +1.8 [+0.9; +2.8], in males and females, respectively). APC for selected cancer sites by gender and province are graphically displayed in **Figure 3**.

Discussion

We analyzed overall and site-specific cancer mortality between 1988 and 2009 in the metropolitan area of Naples and Caserta, southern Italy. Over the considered time frame, the reduction in standardized cancer mortality rates observed in males from this area was paralleled by a more pronounced decrease in the Italian population as a whole. In a subgroup analysis including men aged 65 and older, the decline in cancer mortality found at a national level diverged from the slight, but significant, increase emerging from the metropolitan area of interest. Results from joinpoint analyses showed slight, but significant, downward mortality trends for all cancer sites, independently of gender and specific province. However, in the metropolitan area of Naples and Caserta the overall orientation toward a reduction in cancer mortality appeared to be in antithesis with the slight, but significant, increase in mortality trends for some tumors, i.e., cancers originating from pancreas in both genders, cancers from lung and non-Hodgkin lymphomas in females and colorectal cancers in males.

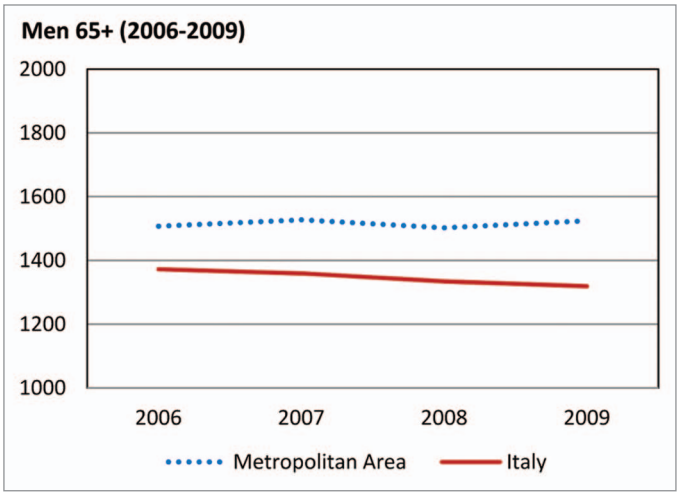

Figure 2. Word standardized mortality rates × 100000 inhabitants in males aged 65 y and older (dotted line, metropolitan area; solid line, Italy) from 2006 to 2009 for all cancer sites.

The general tendency toward decreased cancer mortality observed in the metropolitan area of Naples and Caserta between 1998 and 2009 appeared to be in key with a more favorable trend for Italy overall. Cancer mortality trends for the whole of Italy referred to the time interval between 1998 and 2005 were reported in the 2009 report from the AIRTUM group. Overall, cancer rates decreased significantly in both genders. Percent reductions in mortality rates were –12% and –6% in Italian males and females, respectively. When analyzed by primitive cancer site, deaths by Hodgkin disease, rectum, stomach, and liver cancer were significantly decreased in both genders. Reductions in mortality were also observed for esophagus, lung, and bladder cancer in males, while deaths by colon, breast, uterus, and bone declined in women. Conversely, cancer mortality showed incremental trends in melanoma for males and lung for women. Geographic differences in cancer mortality were reported by macro-areas (i.e., northern, central, and southern Italy), with no specific focus on disparities among provinces.[11]

Cancer mortality in southern Italy between 1999 and 2003 was recently addressed by Bidoli and colleagues in a

Table 1. Joinpoint analysis by cancer site in the provinces of Naples and Caserta, southern Italy. Cancer deaths in males, 1988–2009

	Metropolitan area										Italy
	Naples					Caserta					
Site (ICD X)	No. of deaths	*% of all deaths*	SMR**	APC	(95% CI)	No. of deaths	*% of all deaths*	SMR**	APC	(95% CI)	SMR**
All sites C00–C99	73623	-	171.5	−0.9*	(−1.2; −0.7)	20387	-	163.2	−0.6*	(−1.0; −0.2)	144.1
Head and neck C01–C06, C10–C13	1112	*1.5*	2.4	−1	(−2.4; +0.3)	384	*1.9*	2.9	0.3	(−1.7; +2.3)	2.5
Esophagus C15	647	*0.9*	1.3	−2.9*	(−4.1; −1.7)	221	*1.1*	1.7	−2.4*	(−4.4; −0.2)	2.2
Stomach C16	4206	*5.7*	8.7	−2.5*	(−3.1; −1.8)	1524	*7.5*	11.1	−2.0*	(−2.8; −1.2)	8.7
Intestines C17–C21, C26	6607	*9.0*	16.4	0.08	(−0.5; +0.6)	1980	*9.7*	16.7	+0.9*	(+0.1; +1.6)	16.4
Liver C22	7559	*10.3*	8.8	−0.6	(−1.5; +0.3)	1867	*9.2*	7.5	−1.3	(−2.3; −0.3)	5.0
Pancreas C25	2246	*3.1*	7.0	+1.9*	(+1.0; +2.9)	606	*3.0*	6.3	+1.7*	(+0.06; +3.4)	7.5
Larynx C32	1888	*2.6*	3.6	−3.7*	(−4.3; −3.2)	553	*2.7*	4.3	−1.4	(−3.1; +0.3)	2.4
Lung C33	24380	*33.1*	54.6	−1.4*	(−1.7; −1.1)	6342	*31.1*	49.9	−1.0*	(−1.4; −0.5)	37.9
Skin melanoma C43	786	*1.1*	2.1	0.3	(−1.1; +1.7)	194	*1.0*	2.0	2.7	(−0.5; +6.1)	2.1
Prostate C61	4544	*6.2*	10.0	−0.1	(−0.1; +0.6)	1446	*7.1*	10.9	−0.3	(−1.4; +0.7)	8.7
Bladder C67	4565	*6.2*	9.0	−2.8*	(−3.3; −2.3)	1118	*5.5*	7.7	−1.6*	(−2.6; −0.6)	5.5
Brain C71	2738	*3.7*	4.2	−4.2*	(−6.1; −2.2)	733	*3.6*	4.4	−2.3*	(−4.3; −0.3)	3.8
Hodgkin disease C81	252	*0.3*	0.5	−3.5*	(−5.1; −1.7)	83	*0.4*	0.7	−0.1	(−5.0; +5.0)	0.5
Non-Hodgkin disease C83–C85	1603	*2.2*	4.0	0.01	(−1.0; +1.2)	394	*1.9*	3.1	1.3	(−1.3; +3.9)	3.7
Multiple myeloma C90	737	*1.0*	2.2	1.2	(−0.3; +2.7)	210	*1.0*	1.8	0.2	(−2.2; +2.7)	2.2
Leukemias C91–C95	2247	*3.1*	5.4	−1.2*	(−2.04; −0.3)	699	*3.4*	5.4	−0.5	(−1.8; +0.7)	5.1
Other sites	7506	*10.2*	-	-	-	2033	*10.0*	-	-	-	-

*Only significant joinpoint ($P < 0.05$) were retained in final models for each site. **Standardized mortality rate (world standard rate × 100 000) distribution of cancer types in the provinces of Naples and Caserta and Italy between 2006 and 2009.

Table 2. Joinpoint analysis by primitive cancer site in the provinces of Naples and Caserta, southern Italy. Cancer deaths in females, 1988–2009

	Metropolitan area										Italy
	Naples							Caserta			
Site (ICD X)	No. of deaths	*% of all deaths*	SMR**	APC	(95% CI)	No. of deaths	*% of all deaths*	SMR**	APC	(95% CI)	SMR**
All sites C00–C99	50887	-	93.8	−0.6*	(−0.8; −0.5)	13108	-	85.5	−0.7*	(−1.2; −0.3)	84.2
Head and neck C01–C06, C10–C13	429	0.8	0.9	0.9	(−1.3; +3.2)	104	*0.8*	0.7	0.9	(−1.3; +3.2)	0.7
Esophagus C15	301	0.6	0.6	−1.3	(−3.6; +1.1)	65	*0.5*	0.3	−2.9	(−6.2; +0.4)	0.5
Stomach C16	2048	4.0	4.8	−1.9*	(−2.7; −1.0)	729	*5.6*	5.1	−2.3*	(−3.5; −1.06)	4.3
Intestines C17–C21, C26	6569	12.9	10.5	−1.1*	(−1.6; −0.6)	1930	*14.7*	11.9	−0.3	(−1.3; +0.6)	10.1
Liver C22	4836	9.5	3.6	−2.5*	(−3.1; −1.8)	1060	*8.1*	3.0	−2.7*	(−4.1; −1.4)	1.6
Pancreas C25	2186	4.3	4.5	+2.0*	(+1.2; +2.7)	543	*4.1*	4.5	+2.5*	(+0.7; +4.4)	5.2
Larynx C32	166	0.3	0.3	−0.8	(−3.3; +1.7)	31	*0.2*	0.3	2.6	(−1.3; +6.5)	0.2
Lung C33	4700	9.2	11.5	+2.6*	(+2.0; +3.3)	947	*7.2*	7.5	+1.3*	(+0.1; +2.5)	9.5
Skin melanoma C43	631	1.2	1.3	−0.8	(−2.5; +1.0)	176	*1.3*	1.3	−2.5	(−5.4; +0.4)	1.2
Breast C50	8710	17.1	16.8	−1.0*	(−1.4; −0.6)	2159	*16.5*	15.4	−0.4	(−1.3; +0.4)	15.9
Uterus C53–C55	2715	5.3	4.1	−3.6*	(−4.4; −2.7)	720	*5.5*	4.1	−3.8*	(−5.2; −2.4)	3.5
Ovary C56	1757	3.5	3.7	−0.6	(−1.5; +0.4)	490	*3.7*	3.5	0.5	(−1.3; +2.3)	4.4
Bladder C67	917	1.8	1.3	−2.1*	(−3.4; −0.8)	207	*1.6*	1.3	−2.1	(−4.8; +0.6)	0.9
Brain C71	2286	4.5	3.7	−0.8	(−2.2; +0.5)	632	*4.8*	3.5	−0.6	(−2.9; +1.7)	2.5
Hodgkin disease C81	215	0.4	0.4	−3.4*	(−5.77; −0.86)	63	*0.5*	0.5	−3.6	(−7.3; +0.2)	0.3
Non-Hodgkin disease C83–C85	1428	2.8	2.7	+2.0*	(0.2; +3.7)	321	*2.4*	2.2	0.5	(−1.6; +2.6)	2.2
Multiple myeloma C90	850	1.7	1.8	0.7	(−1.1; +2.7)	178	*1.4*	1.2	−0.4	(−3.6; +2.8)	1.5
Leukemias C91–C95	1946	3.8	3.2	−6.9	(−13.7; +0.4)	526	*4.0*	3.0	−1.7	(−4.0; +0.5)	3.1
Other sites	8197	16.1	-	-	-	2227	*17.0*	-	-	-	-

*$P < 0.05$. **Standardized mortality rate (world standard rate × 100 000) distribution of cancer types in the provinces of Naples and Caserta and Italy between 2006 and 2009.

Table 3. Joinpoint analysis by gender and primitive cancer site in the provinces of Naples and Caserta, southern Italy. Cancer deaths in elderly (65+), 1988–2009

	Elderly (65+)						
	Metropolitan area				SMR**		
Cancer site	No. of deaths	*% of all deaths*	APC	95% CI	Naples	Caserta	Italy
Men							
All cancers	62004	-	−0.3	(−0.6; +0.0)	1527.8	1475.0	1337.5
Stomach	3781	*6.1*	−1.7*	(−2.4; −0.9)	75.7	107.2	82.9
Intestines	6148	*9.9*	0.4	(−0.2; +0.9)	155.1	164.7	159.6
Liver	6331	*10.2*	−0.1	(−0.6; +0.4)	66.0	62.6	44.6
Pancreas	1690	*2.7*	+1.7*	(+0.9; +2.5)	50.3	47.0	65.06
Lung	19718	*31.8*	−0.4*	(−0.7; −0.01)	492.8	452.3	354.3
Non-Hodgkin disease	1000	*1.6*	+1.4*	(+0.3; +2.6)	25.3	24.5	30.6
Women							
All cancers	42434	-	−0.4*	(−0.6; −0.2)	696.5	674.8	661.1
Stomach	2777	*6.5*	−2.2	(−4.5; +0.1)	38.4	50.9	38.1
Intestines	6348	*15.0*	−1.0*	(−1.5; −0.6)	89.5	106.4	90.3
Liver	4517	*10.6*	−1.6*	(−2.2; −1.0)	21.6	20.8	15.8
Pancreas	2045	*4.8*	+1.8*	(+0.9; +2.8)	40.2	40.7	48.7
Lung	3606	*8.5*	+1.6*	(+0.7; +2.51)	74.5	54.8	70.1
Breast	3530	*8.3*	−0.6*	(−1.1; −0.08)	96.3	92.5	97.1
Non-Hodgkin disease	1130	*2.7*	1.5	(−0.3; +3.3)	19.4	15.6	19.5

*$P < 0.05$. **Standardized mortality rate (world standard rate × 100 000) distribution of cancer types in the provinces of Naples and Caserta and Italy between 2006 and 2009.

geographical study specifically focusing on 23 provinces including Naples and Caserta. Despite lower cancer rates observed in southern Italy compared with Italy overall, significant mortality excesses were observed in 7 out of 23 provinces examined, with the highest frequency excesses being reported for liver cancer in males (SMR: +50%, +35%, +30%, and +27% for Bari, Naples, Taranto, and Caserta, respectively) and breast cancer in females (SMR: +17, +16, and +9% for Taranto, Naples, and Bari, respectively).[9]

Over the 1988–1998 time window, standardized mortality rates for all cancer sites in men aged 65 and older from the metropolitan area of interest showed a 13.6% increase, which appeared in contrast with the –2.7% decrease observed for Italy overall. A comprehensive description of cancer mortality among Italian elderly between 1970 and 2008 has been recently performed by Bidoli and colleagues. Mortality data were grouped in quinquennia from 1970–74 through 1995–99, and in 2000–03 and 2006–08 groups. Although the time interval considered is noticeably longer than ours and no referral to macro-areas or specific provinces is made, consistently with our results, the highest peaks in cancer mortality rates among elderly were observed during the quinquennia 1985–89 and 1990–94 in both genders, and declined thereafter. The authors further describe increases in mortality rates between 1995 and 2008 for lung cancer (APC = +0.6%) in females and pancreatic cancer in both genders (+0.6% and 0.9% in men and women, respectively), which are in line with our results.[2]

The overall favorable cancer mortality trends observed in males from the metropolitan area over the past two decades were mainly, though not exclusively, driven by the decline in deaths from tobacco-related cancers. A relevant role was also played by the diminished deaths from esophageal and gastric cancers, tumors from the urinary apparatus (i.e., bladder), and nervous central system (i.e., brain). In females, major determinants of decreasing cancer mortality trends were the drop in death rates from cancers originating from uterus, breast, stomach, liver, and urinary apparatus, as well as by the fall in Hodgkin disease-related deaths. Screening and early diagnosis have profoundly, and almost exclusively, impacted mortality from uterine cancer. Conversely, the decrease in breast cancer deaths observed in Naples and confirmed in women aged 65 y and older must be also interpreted in light of the recent achievements in breast cancer characterization and treatment. Indeed, the remarkably improved knowledge of the molecular features of breast cancer has contributed significantly to orientate modern oncology toward targeted and better tolerated therapies specifically tailored to patient individual needs. In women from the province of Naples, the slight decrease in breast cancer mortality might also reflect improvements in terms of diagnostic delay and socio-economic conditions.[12,13]

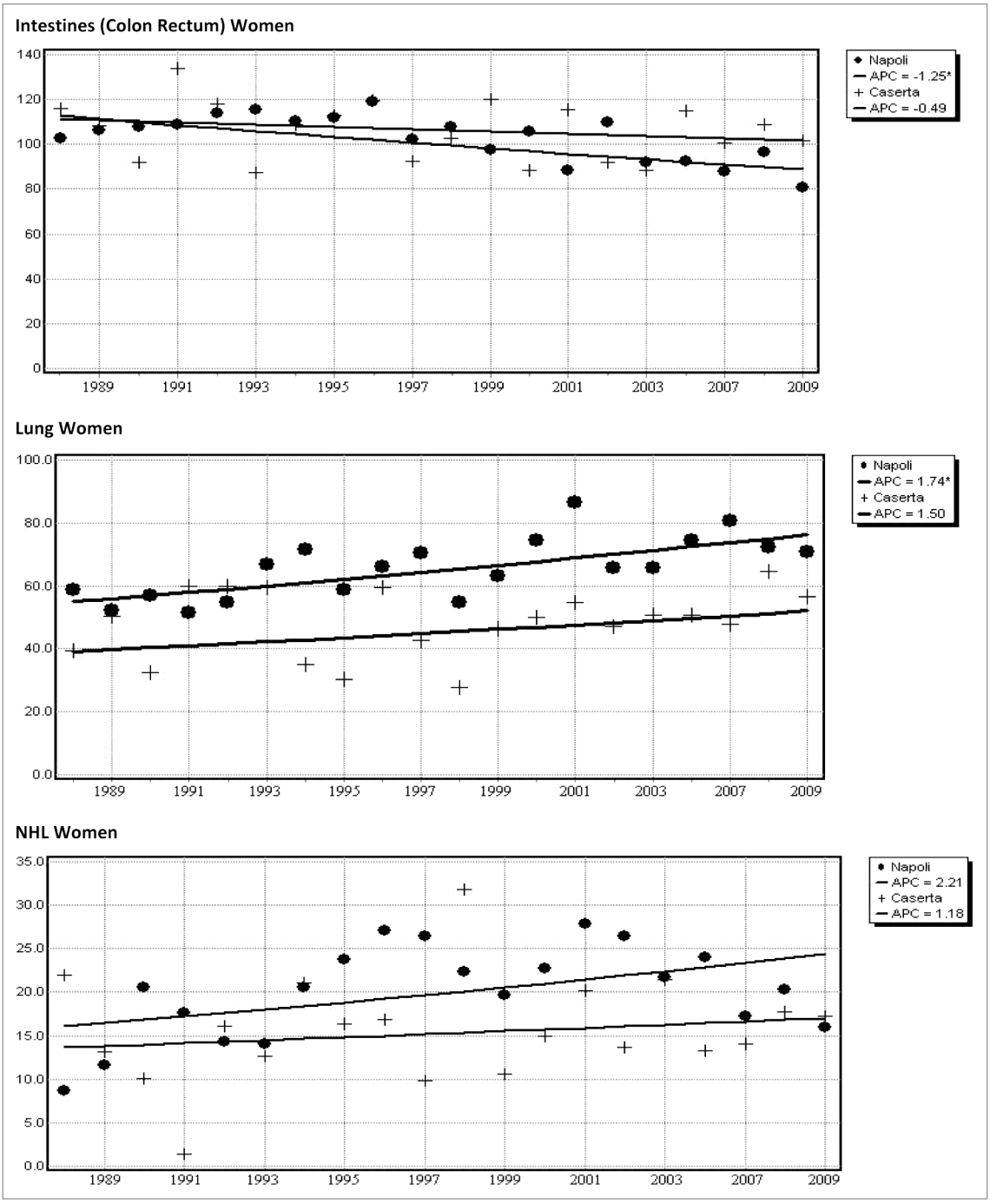

Figure 3. Joinpoint analysis of age-standardized death rates for cancer in Naples and Caserta (metropolitan area) from 1988 to 2009, according to gender and selected cancer site. Naples data points : circle, 65+; solid line, truncated age group 65+ joinpoint model. Caserta data points: cross, 65+; solid line, truncated age group 65+ joinpoint model.

Targeted therapy and personalized medicine, although with somewhat less brilliant results in terms of treatment outcomes, might also largely explain the slight decreasing trends in mortality from colorectal cancer, particularly in women from the area of interest.[14,15] Adoption of standard therapeutic protocols and integrated treatments administered in full accordance with an evidence based approach and current guidelines might eventually explain reduced mortality from Hodgkin lymphoma.[16]

Mortality trends related to liver cancer appeared favorable in women from both the provinces of interest. Liver cancer incidence rates recorded in southern Italy are among the highest all over Europe and are mostly attributable to HBV and/or HCV infections.[9,17] A more punctual and widespread knowledge of the most common risk factors (e.g., unscreened blood transfusions, re-use of needles and syringes, and unprotected sexual intercourses), along with the availability of testing recommendations and vaccine for

HBV have largely contributed to reduce mortality from liver cancer in several western countries, including southern Italy.[9,17-20]

Cancer mortality from colorectal cancer showed a slightly significant increase in men from Caserta (+0.9, +0.1 to +1.6), while only a suggestion for an increasing trend was found in Naples. These data are inconsistent with those referred to the national level and, with respect to the Umbria region, regional panorama.[1,2,21] Differences in lifestyle, particularly concerning a high-fat diet, and prevalence of obesity might at least partly account for the observed discrepancies.[22,23]

We observed increasing mortality trends for pancreatic cancers, which were consistent across the two genders and provinces of interest. Over the past two decades, pancreatic cancer mortality had generally been leveling off worldwide, although slight increases have been observed in southern and central/eastern Europe in recent years. European cancer mortality predictions for the year 2013 preannounce no improvement in mortality rates for pancreatic cancer in both genders, and, if anything, a slight increase is expected. Tobacco smoking, overweight/obesity, and, at a lesser extent, pancreatitis and heavy alcohol drinking are among the better characterized risk factors for this neoplasm. Improved accuracy in the diagnosis and certification of the disease might partly account for the observed trends. Unfortunately, the achievements in diagnostics have not been paralleled by progresses in treatment, with 5-y survival rates currently lower than 5%.[24-27]

In women, mortality for lung cancer showed increasing trends in both the provinces examined. This is consistent with results from previous studies focusing on cancer mortality in Italy.[1,2,11] Bosetti and co-authors have recently addressed the issue of lung cancer mortality in European women between 1970 and 2009 for 33 European countries, including Italy. Their analysis indicates a steady increase in lung cancer mortality trends for European women up to most recent calendar years. Based on their projections to 2015, a further increase in mortality is expected in major European countries. These trends might be largely explained by different patterns of smoking prevalence in subsequent cohorts of women across different European countries.[28,29]

We observed significantly increased cancer mortality trends from non-Hodgkin lymphoma in women from the province of Naples, which were somewhat consistent with the non-significant increases reported for females from Caserta and elderly women aged 65 and older. The available evidence on the association between viral hepatitis and non-Hodgkin lymphoma in the metropolitan area of interest might provide some degree of explanation for this finding. Indeed, in a previous hospital-based case-control study including participants from Naples, HCV infection was associated with a significantly increased risk of non-Hodgkin lymphoma, with the fraction of cases attributable to HCV being 12.4%. These results were consistent with those from a previous study including people from Campania and assessing the association of HCV with a number of tumors correlated with the immune system. HCV infection was associated with greater risk not only for B-cell non-Hodgkin lymphoma, but also for multiple myeloma (odds ratios [OR] and 95% CI: 3.7, 1.9–7.4 and 4.5, 1.9–10.7).[30,31] Nevertheless, existing literature suggests that exposure to polychlorinated biphenyls (PCBs) contributes to non-Hodgkin lymphoma risk.[32,33]

In recent years, the metropolitan area of Naples has become sadly renowned worldwide for the illegal practices of waste dumping. A remarkably high number of uncontrolled sites of urban, toxic, and industrial waste disposal, including land filling and unauthorized incineration, have been traced in this area. Though suggestive of a contributory role of waste exposure in determining health outcomes in the identified areas, including cancer related outcomes, the current available evidence is far from being conclusive.[34,35]

The present study has several strengths. Data presented and discussed relate to a quite wide time frame, namely, the time window between 1998 and 2009. In addition, the appropriateness of the statistical methods used to depict cancer mortality trends and the adjunct of analysis stratified by age, gender and province has further increased the level of detail reached in the analyses performed.

Mortality data were made available by the Italian National Institute of Statistics (ISTAT).[36] Previous studies on the degree of agreement between mortality statistics and clinical diagnoses used for assessment by cancer registries have shown a high degree of reciprocal completeness (over 90%) for both systems and a satisfactory level of concordance.[37] This increases our confidence in the quality of our study results. Future studies might orientate toward the integrative use of secondary databases as potential tools to enhance the detection of cancer related deaths. In these respects, encouraging results have come from previous work focusing on the potentials of a nationwide hospital discharge file in capturing incident breast cancer cases in Italy.[38]

Our study suffers also from some limitations. Data for the years 2004 and 2005 were not available. This somehow interrupts the continuum in the temporal spectrum of our evaluation, which remains however quite wide, since it spans from 1998 to 2009. The use of cancer statistics for mortality evaluation does not allow us to distinguish between endometrial and cervical cancers, which indeed differ significantly by etiopathogenetic aspects and therapeutic management. The limited coverage of the area of interest during the considered time frame refrained us from relying even partially on data from cancer registries.[39] As previously suggested, the use of multiple data sources might have offered the chance to integrate missing data, thus potentially attenuating these limitations and improving the precision of the estimates herein provided. Moreover, the adopted study design is unable to provide any kind of support to the assessment of causal links between a given neoplasm and its risk factors.

In summary, in men from the metropolitan area of Naples and Caserta, the decline observed in SMR between 1998 and 2009 was less marked compared with males from Italy overall. When focusing on men aged 65 and older, the decline in cancer mortality found for Italy overall diverged from the slight increase emerged from the metropolitan area of interest. The overall tendency toward a slight reduction in cancer mortality coexisted with the slight, but significant, increase in mortality

trends for some tumors (NHL, multiple myeloma, pancreas, colon-rectum, among men and lung among women). Factors contributing explanations to the depicted scenario might widely vary by their nature and include lifestyle (e.g., secular trends in smoking, alcohol assumption, diet), overweight and obesity, use of screening procedures, advancements in cancer diagnosis and treatment. By its nature, our study cannot add to the current evidence on the potential causes of the observed cancer mortality trends. However, our findings might help orient public health decision toward specific target populations throughout interventions potential spanning from implementation of screening programs to biomonitoring studies for ascertaining the causal link between exposure to chemical substances in the air, water, soil, food, other potential contaminants, and cancer-related outcomes in the area of interest.

Materials and Methods

Data sources

Population data

Population data are based on the official census of 2001 and referred to the inhabitants of the metropolitan area of Naples and Caserta.[40]

Death certification data

Mortality data were extracted from national death certificates by age (5-y) groups, gender, residence and cause of death. These records were made available by ISTAT for the two provinces of interest and Italy overall. The time window considered spanned from 1988 to 2009. As the International Classification of Diseases (ICD-9 and ICD-10) changed twice from 1998 to 2008, records related to cancer deaths were re-coded according to the Tenth Revision of ICD.[41,42]

Data analysis

From the matrices of certified deaths and resident population, we extracted mortality data related to 5-y age-groups for every calendar year between 1988 and 2009. Data for the years 2004 and 2005 were not available.

Statistical analysis

Age-standardized mortality rates were computed for each 5-y age group, by gender, primitive cancer site and province applying the direct method and using the world standard population. To quantify the recent direction of temporal trends in older populations over time, truncated age-adjusted mortality rates were calculated for people aged 65 y and older. Cancer mortality trends between 1988 and 2009 were analyzed by joinpoint regression, using the program provided by the United States Surveillance Epidemiology and End Results (US SEER). Cancer mortality trends were quantified by estimated APC and related 95% CI. This model is based on linear segments connected at joinpoints that best fit the observed data, that is, the segments that minimize the sum of the square of the differences between estimated and observed data. The time trend is divided into segments: the number of segments depends on the number of joinpoints, fixed arbitrarily a-priori. For k join-points we can have a maximum of k+1 segments with different slopes. The joinpoint year is the point in time when we estimate the trend variation.[43]

Disclosure of Potential Conflicts of Interest

No potential conflicts of interest were disclosed.

Supplemental Materials

Supplemental materials may be found here:
www.landesbioscience.com/journals/cbt/article/26425/

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