

## Estimates of cancer burden in Puglia

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### ABSTRACT

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**Aims and background.** A regional population-based cancer registry that provides incidence and survival data has become active only recently. Since it is important to know the time trends of basic epidemiological indicators to understand the cancer burden in the region, this paper will provide incidence, prevalence and mortality estimates in the region for seven major cancers for the period 1970-2015.

**Methods.** The estimates were obtained by applying the MIAMOD method, a statistical back-calculation approach to derive incidence and prevalence figures starting from mortality and relative survival data. Survival was modeled on the basis of published data from the Italian cancer registries.

**Results.** The incidence rates are estimated to be still increasing for female breast cancer, colorectal cancer in men and skin melanoma in both sexes. By contrast, the incidence rates indicate a decreasing trend for cervix uteri cancer and stomach cancer, the latter both in men and women. For these cancers an analogous trend is observed for mortality, confirming the reduction of the risk factors related to these cancer types. The incidence rates for lung cancer and prostate cancer in men were estimated to rise, reach a peak, and then decrease in the last part of the considered period. Prevalence increased for all the considered cancers except cervix cancer. The increase was striking for breast cancer and less pronounced for stomach cancer in both genders.

**Conclusion.** This paper provides a description of the burden of the major cancers until 2015. The results highlight the need to reinforce effective preventive measures to contrast cancers related to an unhealthy lifestyle and to increase the compliance with organized screening programs to reduce the colorectal and breast cancer burden.

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### Introduction

Puglia is a region in southern Italy with a population of about 4 million<sup>1</sup>. The region consists of 6 provinces: Foggia, Barletta-Andria-Trani, Bari, Brindisi, Taranto and Lecce. Bari is the capital of the region and the largest province, accounting for about 1.2 million inhabitants.

The life expectancy at birth in Puglia is 79.6 years for men and 84.3 years for women<sup>1</sup>; the birth rate and crude mortality rate for all causes are 9.3 and 8.5 per 1,000 population (2009), respectively, resulting in a positive demographic balance<sup>2</sup>. Like all other Italian regions, Puglia's health care is based on a regionally administrated public system. The population is served by almost 70 public hospitals and 37 private clinics; 9 hospitals are provincial, regional or national referral centers. Three specialized cancer hospitals are located in the region: the Scientific Institute for Research and Health Care (IRCCS) "Casa Sollievo della Sofferenza" in San Giovanni Rotondo – Foggia; the IRCCS "Saverio De Bellis" in Castellana Grotte – Bari, and the National Cancer Research Center IRCCS "Giovanni Paolo II" in Bari. In addition, over 30 hospitals and

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60 units provide cancer treatment such as chemotherapy, whereas 10 regional hospitals have the facilities to administer radiotherapy.

Cervical screening is implemented by personal invitation to women aged 25-64 years for a Pap test every 3 years. Mammographic breast cancer screening is mainly focused on women aged 50-69 years who are invited every 2 years and it is also guaranteed to women aged 40-49 years without direct invitation. Citizens with a higher risk of colorectal cancer and their first-degree relatives are invited by their general practitioners to undergo a colonoscopy every 2 years. Those at lower risk and those aged 50-70 years are invited by their general practitioner to undergo a fecal occult blood test every 3 years, followed by colonoscopy in positive cases.

A regional population-based cancer registry has been active since 2009 and is organized in 6 provincial sections. Since the start of 2012 the entire regional population has been covered by registration.

Cancer is the second cause of death in Puglia, with 9,914 deaths in 2008<sup>3</sup>. The regional age-standardized mortality rate is below the southern Italian and national levels (136 *versus* 142 and 143 per 100,000 persons/year, respectively)<sup>4</sup>.

This paper will provide incidence, prevalence and mortality estimates in the Puglia region for the major cancers (lung, breast, prostate, colon-rectum, stomach, cervix uteri and skin melanoma) for the period 1970-2015.

## Material and methods

The MIAMOD method<sup>5-7</sup> was used to estimate the cancer incidence and prevalence. This methodology is based on the mathematical relationships between mortality and prevalence on the one hand and incidence and survival probabilities on the other, for any given disease.

The model parameters for each specific cancer were back-calculated from cancer-specific mortality, general mortality, and population data by age, calendar year and geographical region for the period 1970-2002 and from relative survival data. Mortality and population data were obtained from the Italian National Institute of Statistics (ISTAT)<sup>3</sup>. The cause of death is coded according to the ninth revision of the International Classification of Diseases (ICD-9)<sup>8</sup>. Specific mortality data for the subsequent years, i.e. 2003, 2006 and 2007 (data for 2004-2005 were not yet published by ISTAT), were used to validate the expected mortality projections. Relative survival data for the considered cancers for the period of diagnosis 1985-2002 were obtained from the EURO-CARE-4 study<sup>9</sup>. The data refer to the populations covered by 21 cancer registries in Italy jointly covering about 25% of the national population and they were modeled using, at the level of macro area, a Weibull-type parametric cure model in which the geographical

area and the age of patients were considered as categorical covariates. The way of considering the year of diagnosis (continuous or categorical) and the choice of having a unique parameter or area-specific parameters for the period of diagnosis effect on risk depended on the tumors and the sex<sup>7</sup>. The survival estimates for the southern macro area were assigned to the region. The survival time trend after 2002 was assumed to have the same tendency as that estimated over the observation period 1985-2002 for all cancers except prostate cancer, where survival was assumed to be constant from 2005 onwards.

Table 1 shows the active cancer registries in , with the covered area, the size of the population, the percentage of population older than 65 years, and the data collection period.

All incidence, mortality and prevalence estimates were carried out up to age 99. For cervical cancer, prostate cancer and melanoma additional procedures were applied to account for specific problems related to these sites. The estimates for cancer of the uterine cervix were performed applying a method<sup>10,11</sup> that allowed to correct the observed mortality data provided by official statistics, which are largely incomplete due to misclassification with uterus not otherwise specified (NOS). The methodology could be applied from 1980 onwards because before that year the ICD-8 classification, which did not distinguish uterus NOS, was adopted in the ISTAT statistics. Estimates for this site were carried out up to age 94 years because the distinction of uterus NOS cancer deaths into cervix and corpus uteri cancer deaths in women over 94 years old is not very reliable. Furthermore, for cervical cancer only limited-duration prevalence at 15 years is reported. Indeed, complete prevalence is highly sensitive to the past trends. For cervical cancer, incidence estimates before 1980 are scarcely reliable due to the subsequent spread of non-organized early diagnosis and to the fact that neither mortality nor cancer registry data exist to support reliable modeling assumptions. Simple backward linear extrapolation of the decreasing trend estimated during the 1980s and 1990s may inflate the past incidence level and consequently (due to the high survival) the estimated prevalence of women with a diagnosis of cervical cancer.

For prostate cancer, because of the rapid changes in the recent time trends, more up-to-date mortality data were used in order to capture recent variations that could not be modeled with data up to 2002. Since mortality data for 2004-2005 were not provided by ISTAT, estimates with projections up to 2010 were preliminarily performed by means of the MIAMOD method<sup>12</sup>. The modeled mortality was then used as input for the MIAMOD method.

Projections of the age-specific incidence and mortality rates for melanoma were obtained by linearly projecting the annual percent change of incidence and mortality estimated in the period 2001-2002.

The age-standardized rates were based on the standard European population.

## Results

The number of new cases, deaths and prevalent cases, both the crude and age-standardized incidence and mortality rates and prevalence proportions estimated in Puglia for the year 2012, are presented in Tables 2A and 2B, separately for the 2 sexes. In men, lung cancer was the most frequent cancer type with about 1,781 estimated new cases. The number of new diagnoses for colorectal and prostate cancer was slightly lower (1,610 and 1,507 cases, respectively). The incidence of the other cancers was substantially lower: 378 and 371 estimated new cases of stomach cancer and melanoma, respectively. In the female population, 3,812 new cases of breast cancer and 1,298 new cases of colorectal cancer were expected to be diagnosed during this year. For the other cancers, the number of estimated new diagnoses was considerably lower and ranged between 308 (lung cancer) and 107 (cervical cancer). In males the number of prevalent cases was 8 times higher than the number of estimated new diagnoses for both prostate cancer and melanoma and the number was 5 times higher for colon-rectum cancer. In women the prevalence was 11 times higher than the incidence for melanoma, 9 times for breast cancer, and 6 times for colorectal cancer. The prevalence was about 4 times the incidence in stomach cancer for both genders while in lung cancer it was only twice the incidence for men and about 3 times for women. The highest crude mortality rates were found in lung cancer for men (74 per 100,000) and breast cancer for women (33.8 per 100,000) and the lowest rates were in skin melanoma for both genders (2.7 per 100,000 in men and 1.7 per 100,000 in women) and cancer of the uterine cervix (2.7 per 100,000).

In stomach, colorectal and lung cancer and skin melanoma, all the indicators were higher in men than women; the highest male/female incidence and mortality ratios were reported in lung cancer, i.e. slightly less than 7.3, while the lowest male/female ratios were reported in colorectal cancer (1.7).

The time trends for the 3 indicators over the entire period 1970-2015 are reported in Figures 1-6. They present the age-standardized incidence in men (Figure 1) and women (Figure 2), the age-standardized mortality in men (Figure 3) and women (Figure 4), and the crude prevalence in men (Figure 5) and women (Figure 6). The results will be described below, grouped by cancer site.

### Stomach

The estimates of age-standardized stomach cancer mortality and incidence rates in Puglia displayed a clear downward trend over the whole represented period. The annual incidence rates were estimated to have de-

creased by 38% among men (a decline from 21 per 100,000 in 1970 to 13 in 2015) and 42% among women (from 12 to 7 per 100,000). Mortality for men and women decreased from 19 and 10 per 100,000 in 1970 to 9 and 5 per 100,000 in 2015, respectively.

### Colon and rectum

The colorectal cancer incidence and mortality rates exhibited marked differences between genders in Puglia. The incidence rates in males were estimated to rise in the entire study period (from 18.5 per 100,000 in 1970 to 57 in 2015), while in women the incidence rates increased until the mid 1990s with a less pronounced rate of increase (from 17 per 100,000 in 1970 to 32 per 100,000 in the late 1990s) and then stabilized and from 2010 onwards began to decrease slightly. The mortality trends showed rates initially rising in both genders and declining slightly from the 1990s for women and the 2000s for men. The projected mortality rates in 2015 are still about 50% higher for men and about 10% lower for women than the values observed at the beginning of the 1970s. Colorectal cancer is estimated to be the second most frequent cause of cancer death after lung cancer (in men) and breast cancer (in women) during the period 1980-2015.

### Lung

In males, the lung cancer incidence rates reached a peak during the late 1980s (84.4 per 100,000 in 1988), and decreased thereafter. The incidence rates are forecast to decrease to 59 in 2015. In women the incidence increased until the late 1990s (about 8.7 per 100,000), then leveled off with a slight decline from 2012. Due to the very poor prognosis of this cancer, the mortality trends closely reflect the incidence trends.

### Skin melanoma

The melanoma incidence rates were estimated to increase for both genders. The incidence trends overlapped until the late 1980s but in subsequent years the male rates grew much more rapidly than the female rates, being 55% higher in 2015. In men, the incidence rates increased from 1 to 18 per 100,000 during the period 1970-2015. The mortality rates were low, due to the high survival of melanoma patients. They increased 4-fold among men during the entire study period, while for women they reached a peak during the mid 1990s and tended to slightly decrease thereafter.

### Breast

The breast cancer incidence rates in women increased enormously during the considered period, from 31 per 100,000/year in 1970 to 148 in 2015. The projection for this indicator should be interpreted with caution as it reflects the potential effect of screening rather

than the natural evolution of risk factors. The mortality rate reached a peak in 1989-1990 (26.1 per 100,000/year) and then dropped to a foreseen level of 19.9 per 100,000 in 2015.

#### *Cervix uteri*

Over the study period, the cervix cancer incidence and mortality rates decreased from 14.5 and 8.1 per 100,000 in 1980 to 3.5 and 1.6 in 2015, respectively.

#### *Prostate*

Estimates for prostate cancer showed incidence rates rising until 2003 (from 18.7 to 64.5 per 100,000) and declining thereafter to an expected rate of 42 per 100,000 in 2015. The mortality rates for prostate cancer increased slightly from 1970 to 2000 (from 13.7 to 19.4 per 100,000) and then started to decrease, with an estimated reduction in 2015 of about 40% with respect to the higher level.

#### *Prevalence*

The prevalence increased for all cancers considered except cervix cancer. The increase was striking for breast cancer and less pronounced for stomach cancer in both genders.

## **Discussion**

This paper provides an updated description of the burden of the major cancers in the Puglia region, in terms of time trends through 2015 and point estimates in 2012.

Some preliminary incidence data, available for the period 2003-2007 and for the provinces of Lecce, Taranto<sup>13</sup>, Brindisi and Barletta-Andria-Trani, are compared (Tables 3A-3B) with the regional MIAMOD estimates presented in this paper. The 2 sets of incidence estimates match each other well, even though they were obtained in a completely independent way, as the incidence rates collected by cancer registries were not included in the model estimation procedure.

The incidence rates are estimated to be still increasing for female breast cancer, colorectal cancer in men, and skin melanoma in both sexes. By contrast, the incidence rates indicate a decreasing trend for cervix uteri cancer in women and stomach cancer in both sexes. For these cancers an analogous mortality trend is observed, confirming the reduction of the risk factors related to these cancers.

The lung cancer and prostate cancer incidence rates in men were estimated to increase initially and then decrease in the last part of the study period. In Italy it was

estimated that during 2000 about 91% of lung cancer deaths in males and 55% of lung cancer deaths in females were attributable to tobacco smoking<sup>14</sup>. In 2010 the prevalence of smokers in Puglia was estimated to be 29%, one of the highest among Italian regions<sup>15</sup>. Compared to the results obtained in 2005<sup>16</sup>, it denotes an increase in smoking habit, reaching levels similar to those of the national pool.

Moreover, a wide difference between genders is noticeable<sup>2</sup>: the 2010 prevalence of male and female smokers aged more than 15 years old was 32.7% (above the Italian average of 29.6%) and 13.1% (below the Italian average of 17%), respectively. However, it is remarkable that the smoking prevalence in Puglia among young men (15-24 years) is lower than in Italy (22.9% *vs* 27.4%) and hopefully this will result in a reduced lung cancer incidence over the next decades.

A localized role of industrial carcinogens cannot be ruled out, considering that the Taranto area is characterized by the highest emissions of industrial carcinogens (e.g. PAHs and PCDD/Fs) in the country<sup>17</sup>.

For stomach, colorectal, breast and prostate cancer, diet is one of the most important risk factors<sup>18</sup>. We do not have information about nutritional and dietary characteristics in our region, but the proportion of the Puglia population that was overweight or obese (BMI >25%) was 59% among men and 43% among women in 2010, higher than the national averages (56% and 38%, respectively)<sup>2,19</sup>.

The role of the PSA test in increasing the incidence of prostate cancer is beyond doubt; however, as is the case in other regions, it is not easy to measure the real weight of PSA testing in the area.

Screening programs have a strong impact on the incidence trends of breast, cervical and colorectal cancer. In Puglia, according to the Passi Annual Report<sup>20</sup> the access to Pap tests (at least 1 test in the last 3 years) for 25- to 64-year-old women was estimated to be 62% in the period 2007-2009. In the same report women aged 50-69 years who underwent mammographic examination (at least 1 mammogram in the last 2 years) were 58%, less than the national average (68%) but higher than the proportion estimated for the southern regions in the same period<sup>21</sup>. The access to effective screening tests for colorectal cancer was very low: in the sample of healthy people 50-69 years of age, only 14% stated to have undergone testing (fecal occult blood test or endoscopy) in the last 2 years<sup>22</sup>. The pattern of this cancer in Puglia is still unrelated to preventive strategies, whether mass screening (which started only recently) or spontaneous screening. Our belief is that in Puglia, like other southern regions, there is a silent but steady change in lifestyle towards unhealthy dietary habits and a sedentary lifestyle.

**Table 1 - Puglia population, proportion of the elderly population (1 Jan 2010)<sup>1</sup> and provincial cancer registry sections with their coverage and beginning of activity**

		Population	Population ≥65 years of age %	Coverage %	First year of incidence
Region	Puglia	4,084,035	18	100	
Registry	Bari	1,254,461	18	100	2006
	Barletta-Andria-Trani	391,506	16	100	2006
	Brindisi	403,096	19	100	2006
	Foggia	640,891	18	100	2006
	Lecce	813,556	20	100	2003
	Taranto	580,525	18	100	2006

**Table 2A - Estimated incidence, mortality and prevalence by cancer site for the year 2012 in Puglia. Number of cases and deaths, crude and European age-standardized (age-std) rates per 100,000 person-years and crude prevalence proportion per 100,000 persons. Age 0-99 years, men**

Cancer site	Incidence			Mortality			Prevalence	
	Number of cases	Crude rate	Age-std rate	Number of deaths	Crude rate	Age-std rate	Number of cases	Crude proportion
Prostate	1,507	76.3	47.6	459	23.3	13.6	11,378	576.2
Stomach	378	19.1	13.8	263	13.3	9.4	1,468	74.4
Colon-rectum	1,610	81.6	55.5	629	31.9	21.0	8,131	412.0
Lung	1,781	90.2	63.5	1,454	73.7	50.8	3,807	192.8
Melanoma	371	18.8	16.3	54	2.7	2.2	3,064	155.2

**Table 2B - Estimated incidence, mortality and prevalence by cancer site for the year 2012 in Puglia. Number of cases and deaths, crude and European age-standardized (age-std) rates per 100,000 person-years and crude prevalence proportion per 100,000 persons. Age 0-99 years, women**

Cancer site	Incidence			Mortality			Prevalence	
	Number of cases	Crude rate	Age-std rate	Number of deaths	Crude rate	Age-std rate	Number of cases	Crude proportion
Breast	3,812	182.8	134.1	704	33.8	20.8	34,312	1,645.8
Stomach	269	12.9	7.1	198	9.5	5.1	1,006	48.2
Colon-rectum	1,298	62.3	32.6	523	25.1	12.3	7,831	375.6
Lung	308	14.8	8.7	256	12.3	7.0	845	40.5
Melanoma	196	9.4	7.4	36	1.7	1.1	2,148	103.1
Cervix	107	5.2	4.1	57	2.7	1.9	1,076*	51.7*

\*Limited-duration prevalence at 15 years.

**Table 3A - Estimated incidence by cancer site for the years 2003-2007 in the Lecce, Taranto, Brindisi and Barletta-Andria-Trani (BT) provinces and MIAMOD incidence estimates in Puglia for the period 2003-2006. Age-standardized rates (European population) per 100,000 person-years. Age 0-99 years, men**

Cancer site	Lecce 2003-05	Taranto 2006-07	BT 2006	Brindisi 2006	Puglia - MIAMOD			
					2003	2004	2005	2006
Stomach	16.6	18.2	15.8	13.7	15.6	15.4	15.2	15.0
Colon-rectum	48.1	48.9	52.8	42.9	48.6	49.5	50.3	51.1
Lung	87.5	72.1	60.7	62.7	74.7	73.7	72.5	71.3
Melanoma	7.1	9.8	6.7	5.3	10.1	10.8	11.4	12.1
Prostate	67.1	67.6	65.5	64.8	64.5	63.6	62.3	60.4

**Table 3B - Estimated incidence by cancer site for the years 2003-2007 in the Lecce, Taranto, Brindisi and Barletta-Andria-Trani (BT) provinces and MIAMOD incidence estimates in Puglia for the period 2003-2006. Age-standardized rates (European population) per 100,000 person-years. Age 0-99 years, women**

Cancer site	Lecce 2003-05	Taranto 2006-07	BT 2006	Brindisi 2006	Puglia – MIAMOD			
					2003	2004	2005	2006
Stomach	8.4	7.8	10.6	6.3	8.0	7.9	7.8	7.7
Colon-rectum	34.9	33.9	34.6	30.7	32.8	32.8	32.9	32.8
Lung	10.8	11.4	11.3	10.7	8.8	8.8	8.8	8.8
Melanoma	6.2	8.1	8.3	7.8	5.9	6.1	6.3	6.4
Breast	94.3	97.6	94.7	110.2	97.3	100.0	102.7	105.4
Cervix	6.7	5.7	6.3	5.6	6.0	5.8	5.5	5.3

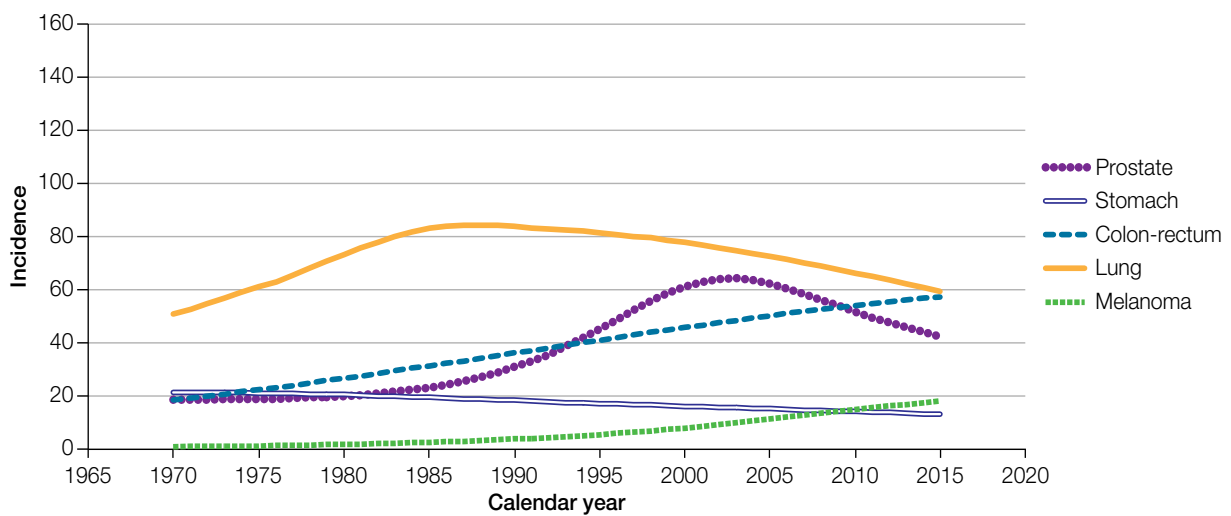


Figure 1 - Incidence estimates by cancer site in Puglia in the period 1970-2015. Age-standardized rates (European population) per 100,000 person-years. Age 0-99 years, men.

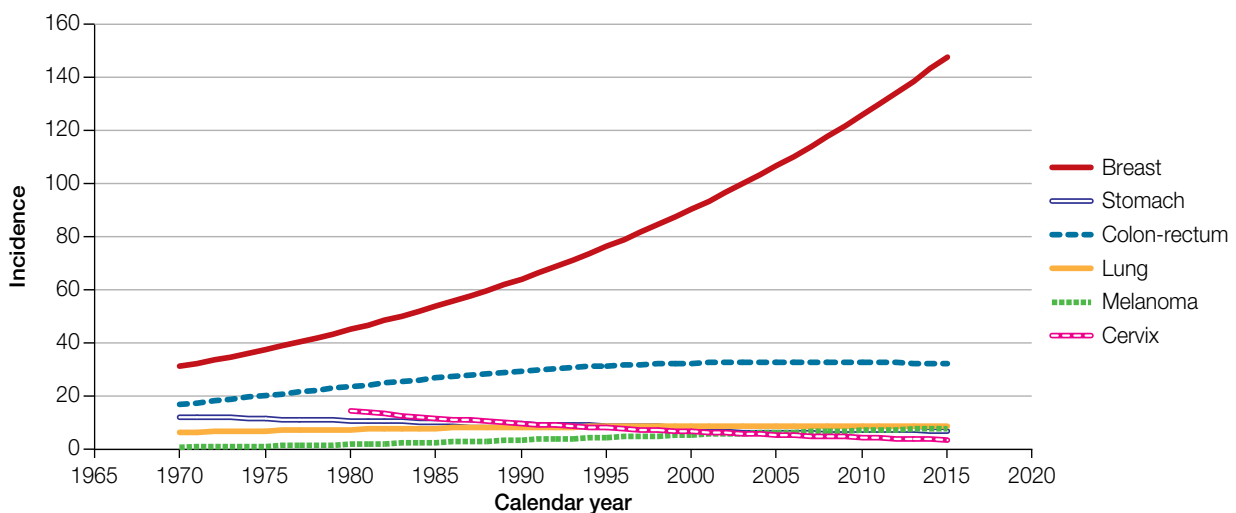


Figure 2 - Incidence estimates by cancer site in Puglia in the period 1970-2015. Age-standardized rates (European population) per 100,000 person-years. Age 0-99 years, women.

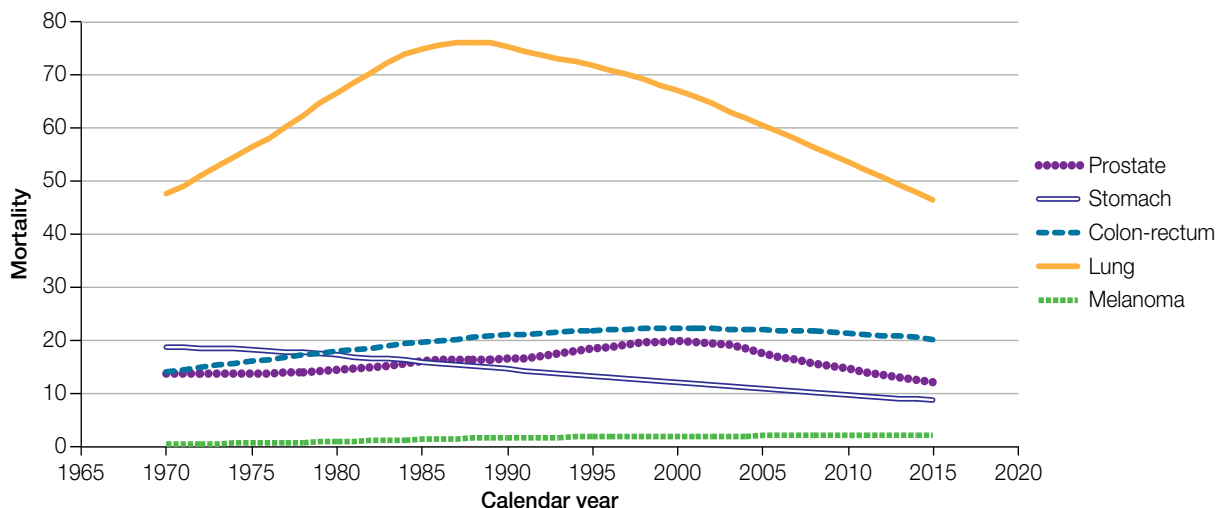


Figure 3 - Mortality estimates by cancer site in Puglia in the period 1970-2015. Age-standardized rates (European population) per 100,000 person-years. Age 0-99 years, men.

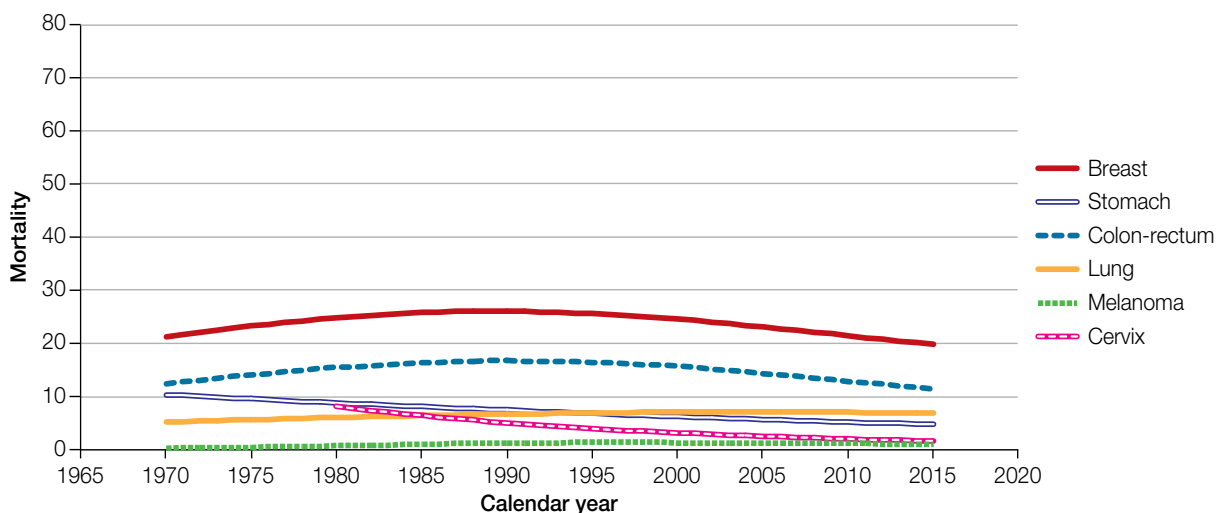


Figure 4 - Mortality estimates by cancer site in Puglia in the period 1970-2015. Age-standardized rates (European population) per 100,000 person-years. Age 0-99 years, women.

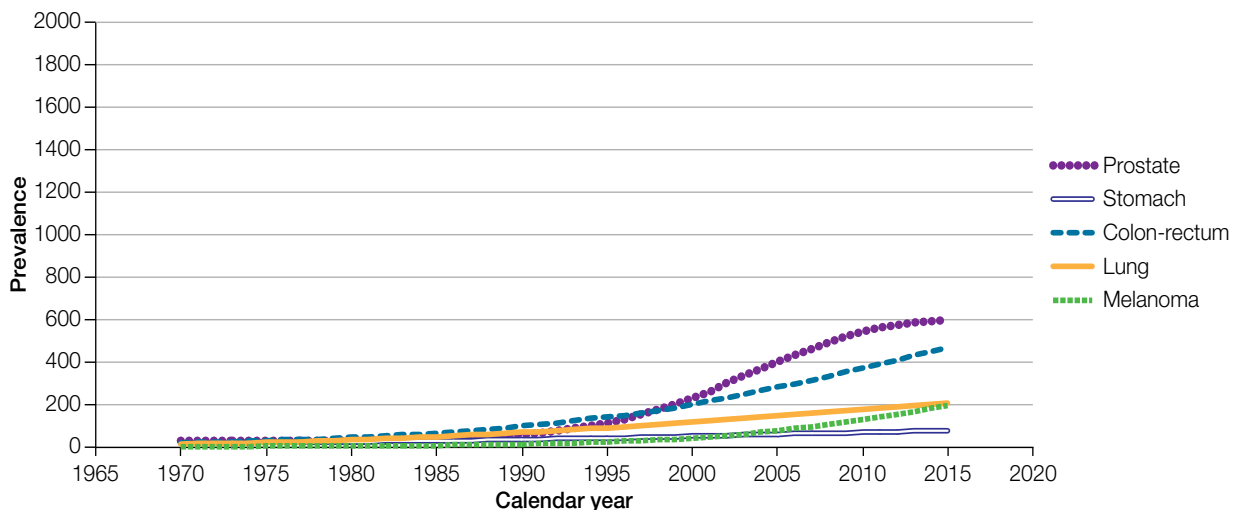
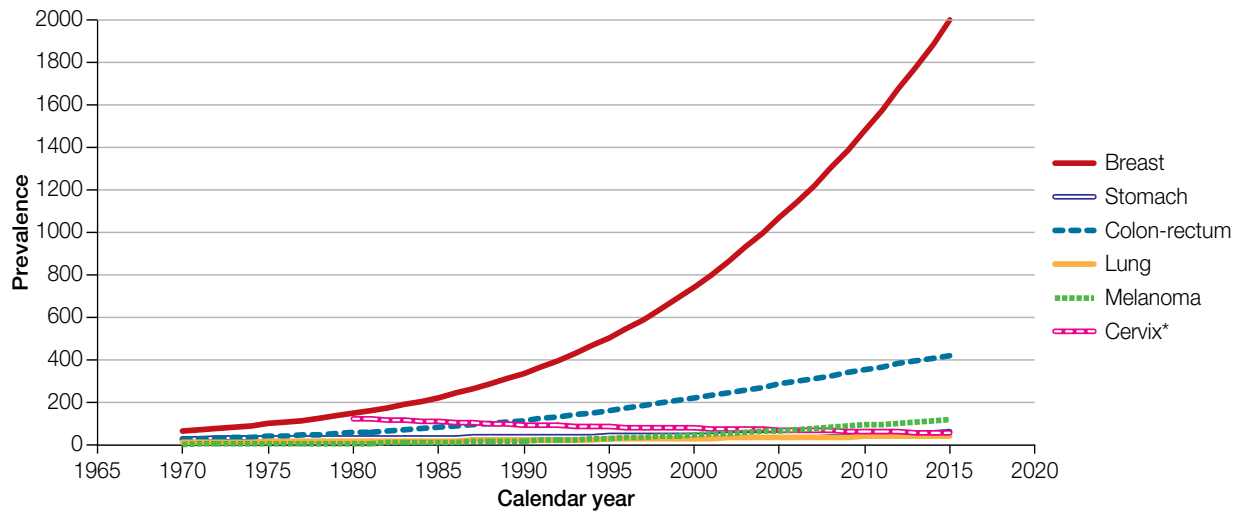


Figure 5 - Prevalence estimates by cancer site in Puglia in the period 1970-2015. Crude proportion per 100,000 persons. Age 0-99 years, men.



\*limited-duration prevalence at 15 years

Figure 6 - Prevalence estimates by cancer site in Puglia in the period 1970-2015. Crude proportion per 100,000 persons. Age 0-99 years, women.

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