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## Estimates of cancer burden in Sicily

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### ABSTRACT

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**Aims and background.** Estimates are complementary epidemiological measures which allow to present data on cancer burden, especially in geographical areas where measurements of cancer occurrence are not supported by exhaustive statistics on incidence, mortality and survival. The aim of this paper is to provide cancer incidence, mortality and prevalence estimates and projections for the major cancers in the period 1970-2015 for the entire region of Sicily.

**Methods.** The estimates were computed by applying the MIAMOD method, a statistical back-calculation approach to derive incidence and prevalence figures starting from mortality and relative survival data. Published data from the Italian cancer registries were modeled in order to estimate the regional cancer survival.

**Results.** In 2012 the most common cancers were breast cancer in women, colorectal cancer in both sexes, and prostate cancer in men, with about 4,000, 3,500 and 3,000 estimated new cases, respectively. The highest crude mortality rates were estimated for lung cancer in men (63.6 per 100,000) and breast cancer in women (30.8 per 100,000) and the lowest for skin melanoma (both sexes) and cancer of the cervix uteri. For colorectal, lung and stomach cancer and skin melanoma, all the indicators were higher in men than women. The prevalence figures in women were more than 9 times the incidence figures for breast cancer and more than 10 times the incidence figures for skin melanoma. The prevalence was twice the incidence for lung cancer in both sexes. The prevalence increased for all the considered cancers except cervical cancer.

**Conclusion.** According to our analyses in Sicily we expect about 14,000 new diagnoses and 5,500 deaths for the major cancer types in a year, while about 92,000 persons with a diagnosis of the considered cancers were alive in 2012. We expect an increase in cancer survival and contemporary aging of the population: both expectations will inflate the cancer prevalence, causing more demand for oncology facilities.

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### Introduction

Sicily is the region with the largest population in southern Italy, with 5,051,075 inhabitants<sup>1</sup>, which is more than 8% of the national population. However, it contributes by a proportion of about 5% (in 2008) to the national gross domestic product<sup>2</sup>, thus representing one of the most deprived Italian regions. Health care is delivered by 9 provincial health authorities (called "Azienda Sanitaria Provinciale", ASP), 3 regional referral hospitals, 2 national referral hospitals, and 3 hospitals related to university medical schools. Sicily counts 26 public hospitals and 55 private hospitals<sup>3</sup>. A total of 262 beds are dedicated to cancer patients<sup>4</sup>, about 1 bed per 19,000 people, which is no less than in the other southern Italian regions. Health care migration for cancer to the north of Italy is an important phenomenon in the Sicily region<sup>5</sup>. Data from the Ragusa Cancer Registry show, for example, that 16% of new breast cancer cases were treated yearly in northern Italy in the early 2000s<sup>6</sup>.

**Key words:** cancer, Sicily, cancer registries, incidence, prevalence, mortality.

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Organized screening for cervical cancer has been implemented since 2008 in 6 provinces (Caltanissetta, Catania, Messina, Ragusa, Siracusa and Trapani), while 2 breast mammography screening programs and no colorectal cancer screening were active in the same year<sup>7</sup>.

At the beginning of the year 2012, 82% of the regional population were covered by cancer registration. Four population-based general cancer registries provided incidence and survival data by the time of this study, all of them covering entire provinces (Palermo, Ragusa, Siracusa, Trapani). A further specialized cancer registry (breast) is active in the Palermo province.

Cancer is the second cause of death in Sicily, with about 11,000 cancer deaths per year in the period 2004-2008<sup>8</sup>. The Sicilian age-standardized mortality rates in 2006 were 115.6 per 100,000 in men and 77.7 per 100,000 in women<sup>8</sup>. Even if these figures were slightly lower than the mean mortality rates in southern Italy<sup>9</sup>, such measurements have to be taken into account for planning primary care and facing the social needs related to cancer patients. They also need to be considered in planning interventions for primary prevention in order to reduce the risk of people developing cancer and dying of the disease.

This paper will provide estimates of the basic epidemiological indicators (incidence, prevalence and mortality) up to 2015 in the Sicily region for the following major cancers: lung cancer, breast cancer, prostate cancer, colorectal cancer, stomach cancer, cervical cancer and skin melanoma.

## Material and methods

Table 1 reports the list of cancer registries active in Sicily, with the respective area and size of the population covered, the corresponding coverage of the regional population, the percentage of people older than 65, and the data collection period. Mortality data for all cancers, general mortality and population data by age, calendar year and geographical region for the period 1970-2002 were obtained from the Italian National Institute of Statistics (ISTAT)<sup>10</sup>.

Relative survival data for the considered cancers referring to the period of diagnosis from 1985 to 2002 were obtained from the EURO CARE-4 study<sup>11</sup>. They refer to the populations covered by 21 cancer registries in Italy, jointly covering about 25% of the national population.

The MIAMOD method<sup>12-14</sup> was used for estimation of incidence and prevalence. This statistical method is based on a back-calculation approach to estimate and project the morbidity of chronic irreversible diseases starting from mortality and patient survival. The method relies on the mathematical relationships between mortality, prevalence, incidence and survival. The model estimation is based on mortality data from ISTAT for the period 1970-2002, with cause of death

coded according to the ninth revision of the International Classification of Diseases (ICD-9)<sup>15</sup>. 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 of cancer patients was estimated from observed cancer registry data by means of parametric cure models of the Weibull type at the level of macro area. Geographical area and patients' age were considered categorical covariates in the survival model. The covariate year of diagnosis for each site and sex was parameterized as continuous or categorical – and as unique for all areas or variable by area – according to the pattern of observed survival data<sup>9,12,13</sup>. The survival estimates for southern Italy were used to carry out the analysis for the Sicily 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 cancer sites except prostate, for which the survival was assumed to be constant from 2005 onwards.

All incidence, mortality and prevalence estimates were carried out up to age 99. For cervical cancer, prostate cancer and skin melanoma additional procedures were applied to account for problems specifically related to these sites. The estimates for cervix cancer were performed after having estimated the regional cervical cancer mortality using a specific methodology<sup>16,17</sup> that allows to correct the observed mortality data, which are largely incomplete due to misclassification of a proportion of cervical and corpus uteri cancers into cancer of the 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. Corrected mortality figures were used as input data for incidence and prevalence estimates by the MIAMOD method. Estimates for cervical cancer were carried out up to age 94 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 unreliable 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 mor-

tality data for 2004-2005 were missing, mortality estimates with projections up to 2015 were preliminarily performed by means of the PIAMOD method<sup>18</sup>. The modeled mortality was then used as input for the MIAMOD method.

Projections of incidence and mortality rates for skin melanoma were obtained by linearly projecting the annual percent change of age-specific incidence and mortality estimated in the period 2001-2002. Crude and age-standardized rates were obtained by age-specific rates. The age-standardized rates were based on the standard European population.

## Results

The number of cases and both the crude and age-standardized incidence and mortality rates and prevalence proportions estimated in Sicily for the year 2012 are presented in Tables 2A and 2B for men and women, respectively. Prostate cancer was the first cancer in the male population, with about 3,000 estimated new diagnoses in a year, while breast cancer was the most common cancer in women, with a little over 4,000 new cases diagnosed in 2012. The incidence for the other cancers and in both sexes ranged between approx. 3,400 (colon-rectum) and 94 (cervix uteri) estimated new cases. The prevalence figures in women were more than 9 times the incidence for breast cancer and more than 10 times for skin melanoma. Prevalence was double the incidence for lung cancer in both sexes. The highest crude mortality rates were estimated for lung cancer in men (63.6 per 100,000) and breast cancer in women (30.8 per 100,000), and the lowest for skin melanoma (both sexes) and carcinoma of the cervix uteri. For colorectal cancer, lung cancer, stomach cancer and skin melanoma, all the indicators were higher in men than women; the highest ratio was reported for lung cancer, slightly more than 3.5, and the lowest for colorectal and gastric cancers (between 1.2 and 2.2).

The time trends of the 3 indicators over the period 1970-2015 are shown 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

For stomach cancer the incidence and mortality trends were estimated to be clearly decreasing during the whole studied period. In men the age-standardized incidence and mortality rates decreased from 29 and 26 per 100,000 in 1970 to 15 and 9 in 2015, respectively. The trends in women were similar and the rates were always lower in women than in men.

### Colon and rectum

For colorectal cancer the male incidence rates were estimated to rise until the year 2015 (64 per 100,000), while the female incidence rates were estimated to rise until the year 2000 (33 per 100,000) and to drop slightly thereafter (30 per 100,000 in 2015). Rates were always lower in women than in men. After 2010, colorectal cancer is estimated to have higher incidence than lung cancer, and to become the second most frequent malignancy in the Sicilian male population, after prostate cancer. The mortality trends were increasing in both sexes up to the late 1990s. During the final period considered they leveled off to around 23 per 100,000 in men and started to decrease in women. Female colorectal cancer projections estimate similar mortality rates in 2015 (10 per 100,000) to those observed in 1970.

### Lung

The lung cancer incidence rates in men reached their peak during the late 1990s (with a maximum equal to 69 per 100,000 in 1997-98) and decreased thereafter. In women, they steadily increased up to 12 per 100,000 in 2015. Due to the very poor prognosis of this cancer, the mortality trends closely mimic those estimated for incidence. In women, lung cancer was estimated to have been the third most frequent cause of cancer death since 1994, after breast and colorectal cancer.

### Skin melanoma

The melanoma incidence rates were estimated to increase uniformly for both sexes after 1985. In men, we estimated an increase from 2 to 12 per 100,000/year during the period 1970-2015. The trend in women was similar, with rates about 30% lower than in men. The mortality rates were low, due to the high survival of skin melanoma patients. They reached a peak in women during the late 1990s and tended to decrease slightly thereafter; in men they slightly increased up to 2015.

### Breast

Breast cancer in women was estimated to rapidly increase from 30 per 100,000 in 1970 to about 120 per 100,000 in the early 2010s. Projections for breast cancer incidence are to be taken with caution, as this indicator reflects more the impact of screening activities than the natural evolution of risk factors. Our projections, based on observations up to 2002, foresee a continuing increase up to 2015, even though the rise seems to be less pronounced in the observed data. Mortality rates reached a peak (26 per 100,000) in 1990 and then dropped continuously to a foreseen level of 18 per 100,000 in 2015.

### Cervix uteri

During the study period, the cervix cancer incidence and mortality rates dropped substantially, reaching the

lowest figures among the malignancies considered: 2 and 1 per 100,000, respectively, in the year 2015.

### *Prostate*

For prostate cancer, the incidence trend was estimated to increase during the period 1985-2005 from 20 per 100,000 to 71 per 100,000/year. Thereafter, the age-standardized incidence rates are expected to stabilize or increase slightly, reaching a rate of 75 per 100,000 in 2015. The prostate cancer incidence surpassed the lung cancer incidence in the early 2000s. Mortality for prostate cancer was slightly increasing from 1970 to 2005 and then remained stable up to the year 2015.

### *Prevalence*

The prevalence increased for all cancers considered except cervix cancer. The rise was less pronounced for stomach cancer due to the impressive drop in incidence, whereas the rise in prevalence was striking for breast and prostate cancer. It is interesting that an opposite trend was noted in the mortality rates, which declined for all considered cancer sites except lung cancer in women.

## **Discussion**

The cancers considered in this paper represent the majority (60%) of all malignancies at the national level<sup>19</sup>, so our estimates address a large part of the cancer burden in the region. In 2012, we expect in Sicily about 14,000 new diagnoses and 5,500 deaths from the major cancer types, while about 92,000 persons with a diagnosis of the studied cancers were alive. The great majority (84%) of the estimated prevalent cases were affected by breast, colorectal and prostate cancers.

The estimated incidence rates were validated through comparison with the observed rates in the provinces covered by the cancer registries of Ragusa, Siracusa and Palermo (for breast cancer), which have a sufficiently long period of observation. The comparison between the estimated Sicilian incidence and the data of these registries, which are available in the AIRTUM database, showed a good match over the period covered by registration. The results of the validation procedures will be extensively presented in a specific paper.

The age-standardized incidence rates are estimated to be still rising for breast and lung cancer in women, colorectal and prostate cancer in men, and skin melanoma in both sexes. By contrast, the rates have been declining for cervix and stomach cancer. The incidence increased, peaked, then decreased for lung cancer in men and colorectal cancer in women. Differently from what has been reported in many Western countries<sup>20-22</sup>, no decrease in incidence was estimated during recent years in the Sicilia region for prostate cancer.

The major risk factor affecting the observed trend is smoking. Smoking is related to lung, stomach and cervical cancer<sup>23,24</sup>. The prevalence of smoking in Italy has been decreasing among men since the 1970s. By contrast, the smoking habit has been rising in women, approaching the proportion of male smokers in 1990s. The time trend of smoking prevalence in Sicily has been decreasing in men, from 40% in 1993 to 32% in 2010, and is stable in women at around 15% in the same period. In 2010 the total prevalence of Sicilian smokers was estimated to be the second highest, after Campania, among the southern Italian regions (23% and 26%, respectively in Sicily and in Campania)<sup>25</sup>.

For stomach, colorectal, breast and prostate cancer, diet is the most relevant risk factor<sup>24,26</sup>. We do not have information about food consumption trends by region, but the Passi survey provides important indications on dietary habits and their effects<sup>27</sup>. This study has shown at the national level a tendency to increasing consumption of energy-dense foods and sugary drinks, along with a reduction of the consumption of salted or smoked preserved foods, an important risk factor for stomach cancer<sup>27</sup>. In 2008, about 1 of 2 adults were overweight or obese in Sicily (37% of women and 62% of men)<sup>28</sup>. The same survey reported that almost all adults (96%) eat fruit daily: 56% have 1 or 2 servings a day, while only 8% of the interviewed adults followed the recommendation to eat fruit at least 5 times a day<sup>28</sup>.

According to the EPIC study, the energy intake from macronutrients observed in the Ragusa cohort of adults showed that the proportions of protein (15%), total fat (33%) and total carbohydrates (49%) were slightly different with respect to the other participating Italian centers, in that there was higher carbohydrate and lower animal protein intake<sup>29</sup>.

Screening programs have had a strong impact on the incidence trends of breast, cervical and colorectal cancer since their implementation. The ninth report of the National Center for Screening Monitoring<sup>30</sup> and the National Survey Passi (Passi, Sicily)<sup>27</sup> provide information about the access to screening for the years 2008 and 2009. The access to screening Pap tests for 25 to 64 year-old women was quite low (20%)<sup>30</sup>; however, 62% of adult women had a spontaneous Pap test in the 3-year period before the survey (Passi, Sicily)<sup>28</sup>. In 2008-2009, almost 160,000 women in Sicily aged 50-69 years (48%) were invited to have a screening mammogram; only 38% of these women actually attended the examination<sup>30</sup>. This datum is in agreement with the Passi survey reporting 35% of women (50-69 years of age) having a preventive mammographic exam in the last year and 28% never undergoing the exam<sup>27,28</sup>.

As in several Western countries, also in Sicily the incidence of skin melanoma is increasing<sup>31,32</sup>. Historically, the melanoma incidence in the region and the entire southern part of Italy was low. Factors contributing to the recent increase include ultraviolet light exposure,



greater public awareness of the warning signs of skin melanoma, and increased attention to early diagnosis by clinicians<sup>33</sup>.

The huge increase in prostate cancer incidence was largely due to opportunistic screening, mainly through PSA testing, which started in Sicily in the late 1980s. Since the rise in incidence is not accompanied by a corresponding reduction in mortality, which was quite stable since 2005, it is likely that much of the prostate cancer incidence rise comes from early diagnosed lesions, including overdiagnosis. The prostate cancer incidence in Sicily is expected to rise up to 2015, differently from what is observed in northern Italian regions and in many Western countries including the US and Nordic countries, where the incidence started to decline around 2000<sup>20-22</sup>.

Since the early 1990s the mortality rates for all considered cancers, except lung cancer in women, have been declining. Mortality depends on incidence. For a cancer like lung cancer, with very few therapeutic options, the mortality rates are very close to the incidence rates. Monitoring and paying attention to smoking intervention programs and to compliance with antismoking law may have contributed to the decrease in lung cancer incidence.

Mortality is also related to survival. Early diagnosis for those cancers that benefit from effective therapy given to patients with localized disease is likely to have also contributed to the observed decline in mortality rates. Breast, cervical and colorectal cancer benefit from early

diagnosis. Screening programs have to be organized in the entire region and their efficacy should be systematically monitored according to the recommendation by the Ministry of Health<sup>34</sup>.

The measure of the burden of these cancers for treatment, clinical follow-up, palliation and social disabilities is given by their prevalence, which represents an important indicator for the organization of health services. In this paper, prevalence trends for the major cancers are given for the first time for the Sicily region. Tables 2A and 2B show that the greatest demand for health care resources comes from female breast and colorectal cancers. About 40,000 women and 20,000 persons, respectively, with a previous diagnosis of breast and colorectal cancer are estimated to live in Sicily.

To conclude, we believe that prevention is the only way to save further lives and preserve health resources. In Sicily substantial diagnostic and therapeutic resources have contributed to the decreasing mortality rates. Due to the benefit of early diagnosis, to the screening programs implemented in 2011 in many Sicilian provinces, to the installation of new radiotherapy units and partly to improvement of therapeutic effectiveness, cancer survival is expected to increase in the next years. This phenomenon, added to population aging, will inflate the cancer prevalence. Facing the increasing demand for oncology services is one of the major challenges of the Sicily region.

**Table 1 - Sicily population, proportion of the elderly population in 2011 and cancer registries with their coverage and first year of incidence**

		Population	Population ≥65 years of age %	Coverage of the region %	First year of incidence
Region	Sicily	5,051,075	18	80	
Registry	Catania-Messina	1,743,838	18	34	2003
	Palermo, general	1,249,577	18	25	2003
	Ragusa	318,549	18	6	1981
	Siracusa	402,271	18	7	1999
	Trapani	436,624	20	8	2002
	Palermo specialized breast cancer	646,891	19	40% of regional female population	1999

**Table 2A - Estimated incidence, mortality and prevalence by cancer site for the year 2012 in Sicily. 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	2,840	117.3	74.2	725	29.9	17.0	17,766	733.6
Stomach	477	19.8	15.0	321	13.3	9.7	1,903	79.0
Colon-rectum	2,142	89.0	61.1	830	34.5	22.8	10,744	446.2
Lung	1,879	78.0	56.6	1,532	63.6	45.1	4,231	175.6
Melanoma	321	13.3	11.4	49	2.0	1.6	2,629	109.2

**Table 2B - Estimated incidence, mortality and prevalence by cancer site for the year 2012 in Sicily. 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	4,120	160.8	118.8	790	30.8	18.8	39,678	1,548.4
Stomach	299	11.7	6.8	220	8.6	4.8	1,217	47.5
Colon-rectum	1,386	54.1	30.3	564	22.0	11.5	9,410	367.2
Lung	482	18.8	11.5	396	15.4	9.1	1,282	50.0
Melanoma	200	7.8	6.3	35	1.4	0.9	2,165	84.5
Cervix	94	3.7	2.7	57	2.2	1.4	1,043*	40.8*

\*Limited-duration prevalence at 15 years.

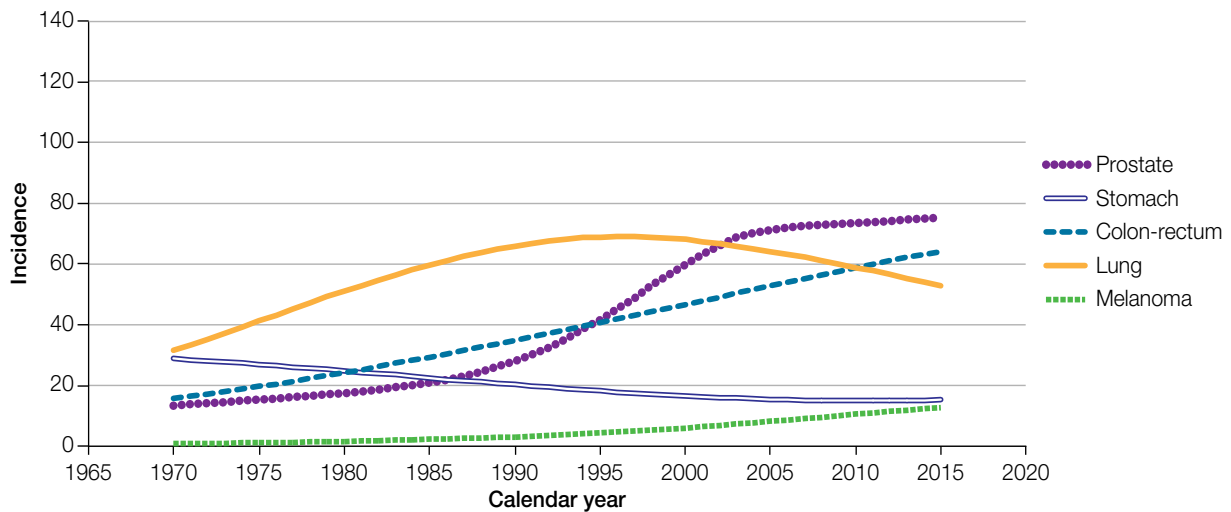


Figure 1 - Incidence estimates by cancer site in Sicily in the period 1970-2015. Age-standardized rates (European population) per 100,000 person-years. Age 0-99 years, men.

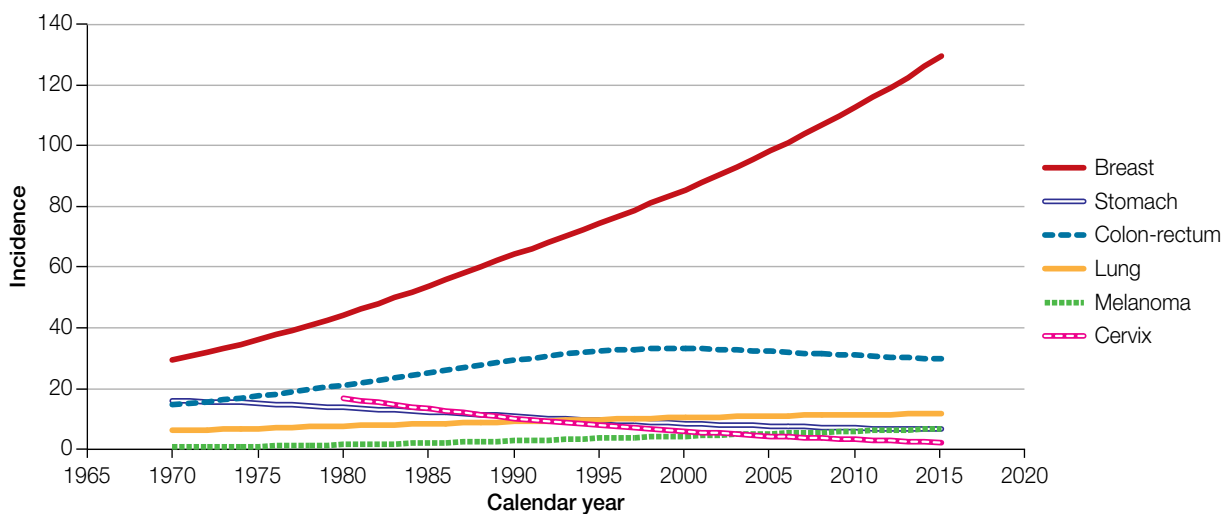


Figure 2 - Incidence estimates by cancer site in Sicily in the period 1970-2015. Age-standardized rates (European population) per 100,000 person-years. Age 0-99 years, women.

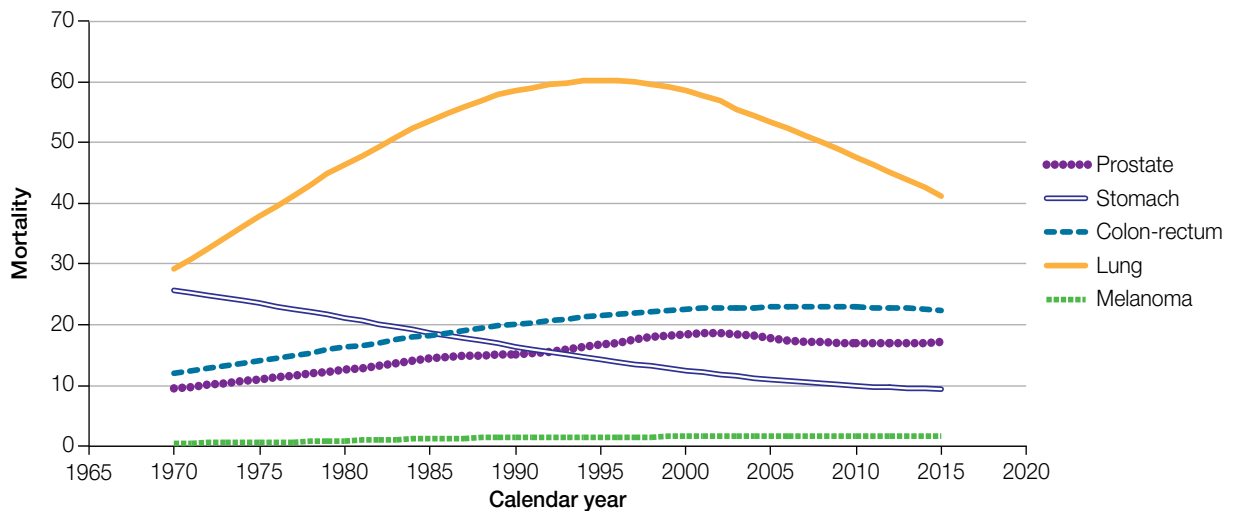


Figure 3 - Mortality estimates by cancer site in Sicily in the period 1970-2015. Age-standardized rates (European population) per 100,000 person-years. Age 0-99 years, men.

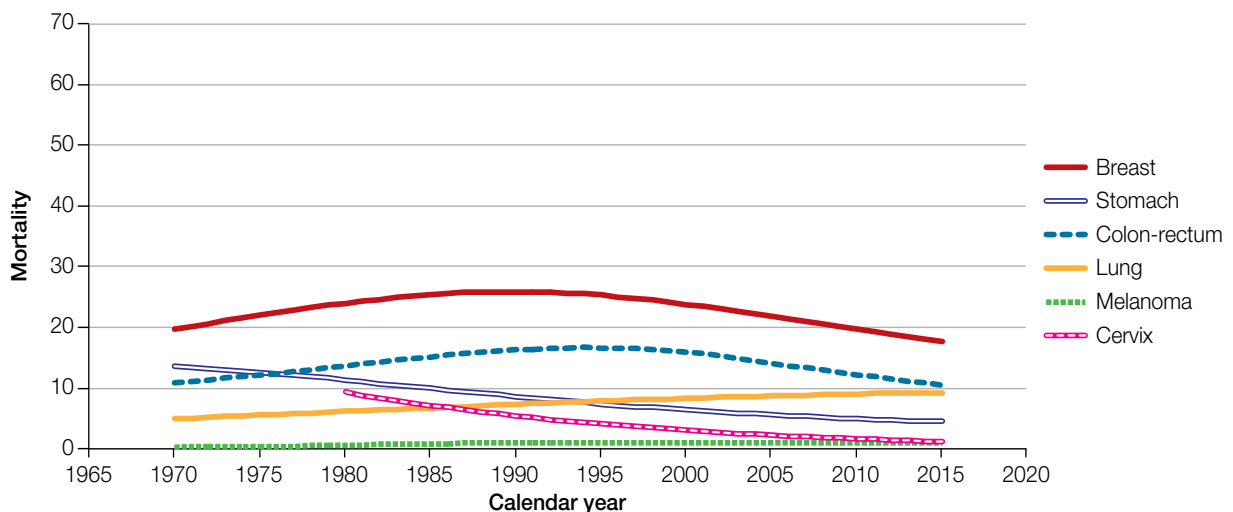


Figure 4 - Mortality estimates by cancer site in Sicily in the period 1970-2015. Age-standardized rates (European population) per 100,000 person-years. Age 0-99 years, women.

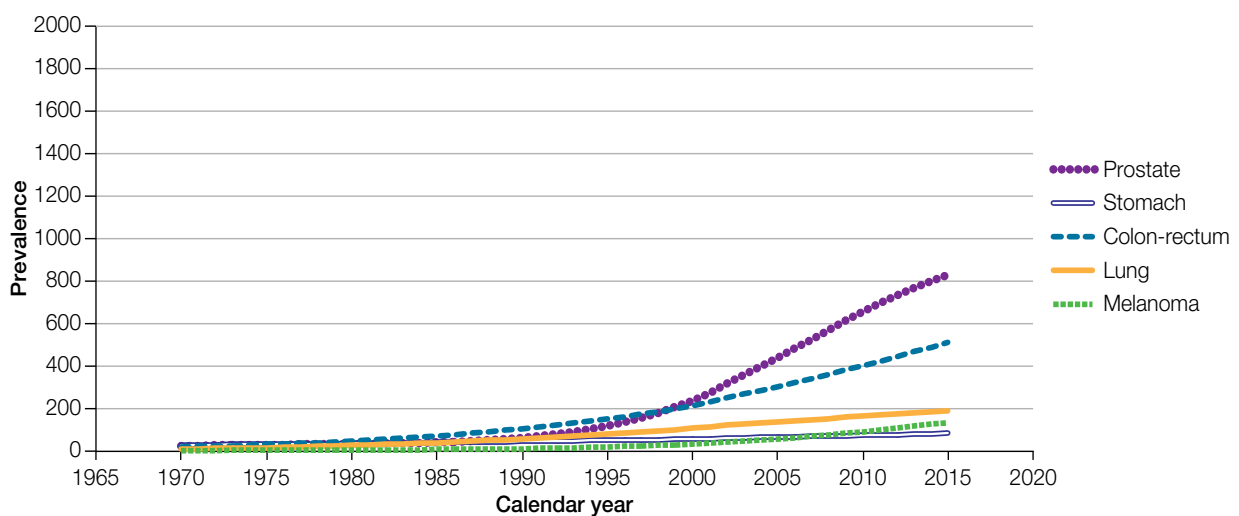


Figure 5 - Prevalence estimates by cancer site in Sicily in the period 1970-2015. Crude proportion per 100,000 persons. Age 0-99 years, men.

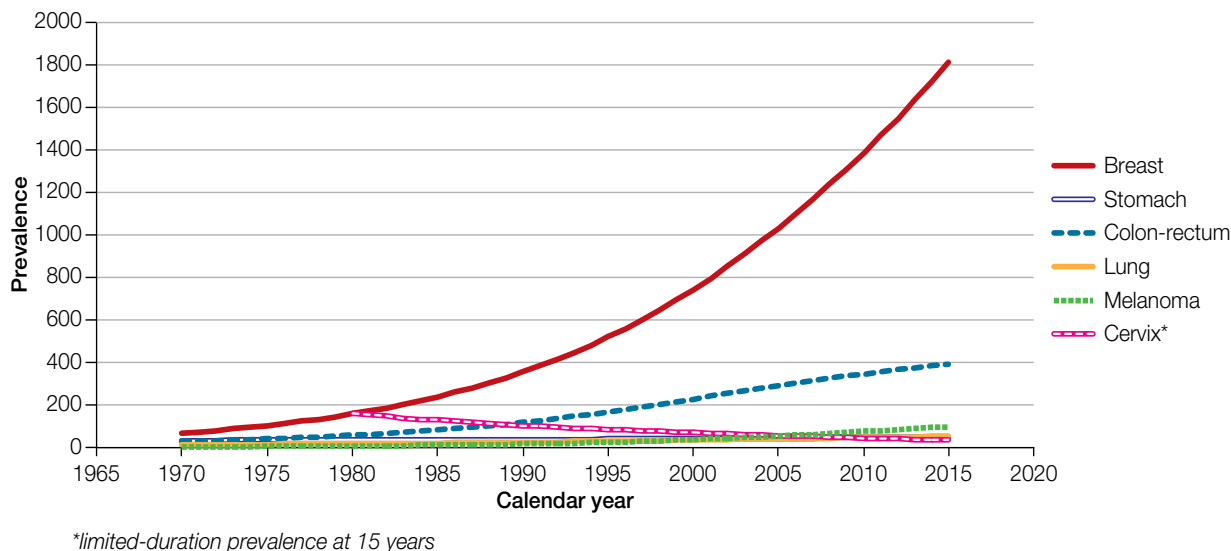


Figure 6 - Prevalence estimates by cancer site in Sicily in the period 1970-2015. Crude proportion per 100,000 persons. Age 0-99 years, women.

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