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Estimates of cancer burden in Sardinia

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ABSTRACT

Aims and background. Cancer registration in Sardinia covers 43% of the population and started in 1992 in the Sassari province. The aim of this paper is to provide estimates of the incidence, mortality and prevalence of seven major cancers for the entire region in 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. Estimates were compared with the available observed data.

Results. In 2012 the lowest incidence was estimated for stomach cancer and melanoma among men, with 140 and 74 new cases, respectively, per 100,000. The mortality rates were highest for lung cancer and were very close to the incidence rates (77 and 95 per 100,000, respectively). In women, breast was by far the most frequent cancer site both in terms of incidence (1,512 new cases) and mortality (295 deaths), followed by colon-rectum (493 cases and 201 deaths), lung (205 cases and 167 deaths), melanoma (106 cases and 15 deaths), stomach (82 cases and 61 deaths), and uterine cervix (36 cases and 19 deaths). The highest prevalence was estimated for breast cancer (15,180 cases), followed by colorectal cancer with about 7,300 prevalent cases in both sexes.

Conclusion. This paper provides a description of the burden of the major cancers in Sardinia until 2015. The comparisons between the estimated age-standardized incidence rates and those observed in the Sassari registry indicate good agreement. The estimates show a general decrease in cancer mortality, with the exception of female lung cancer. By contrast, the prevalence is steeply increasing for all considered cancers (with the only exception of cancer of the uterine cervix). This points to the need for more strongly supporting evidence-based prevention campaigns focused on contrasting female smoking, unhealthy nutrition and sun exposure.

Key words: cancer, cancer registries, incidence, prevalence, mortality, Sardinia.

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Introduction

Sardinia is an autonomous region with special status located in the southwest of the Italian peninsula, with a population of 1,675,411 in 2011[1], an area of about 24,090 km^2, and a population density of 69.5 per km^2. The main economic activities are chemical industry, tourism, agriculture, and port activity. The chemical industry developed in the late 1950s and early 1960s; the industrial settlements were built in the provinces of Sassari, Nuoro and Cagliari. For several years the industries have been in a crisis and they have left the sites of settlement strongly polluted. Health care in Sardinia is efficient and the degree of health care migration to other parts of the country is very limited (approx. 5%).

In Sardinia there are currently 11 public regional hospitals and 8 private hospitals, with 3 oncology departments in Sassari, Nuoro and Cagliari. Twelve outpatient on-

cology services are active and there are 5.4 beds per 100,000 outpatient oncology residents and 3 services (1 per 557,468 population) for radiation therapy.

Cancer screening programs (for breast, cervical and colon cancer) have recently been initiated; they do not cover the entire region but have expanded patchily. There are 2 cancer registries in the provinces of Sassari and Nuoro covering just over 40% of the population of the island. In 2008 the age-standardized mortality rates for all malignant cancers were 356 and 189 per 100,000 for men and women, respectively[2]. Table 1 shows the coverage of the 2 active cancer registries in Sardinia.

The aim of this paper is to provide the figures for the basic epidemiological indicators – incidence, prevalence and mortality – in Sardinia for the major cancers (lung, breast, prostate, colon-rectum, stomach, cervix uteri and skin melanoma) for 2012 and time trends up to 2015.

Material and methods

Incidence, mortality and prevalence estimates were obtained by applying the MIAMOD statistical back-calculation method to survival and mortality data. The MIAMOD method, as described elsewhere in detail[3,4], was applied to estimate the absolute number of incident cases, deaths and prevalent cases, crude and age-standardized (using the standard European population) incidence and mortality rates (per 100,000 person-years), and prevalence proportion (per 100,000) for the period 1970-2015. All estimates were carried out up to age 99 years.

Briefly, the MIAMOD method relies on the mathematical relationships between mortality, prevalence, incidence and survival and the model estimation is based on mortality data and relative survival estimates. Mortality data for all cancers, general mortality and population data by age, calendar year, and geographical area for the period 1970-2002 were obtained from the Italian National Institute of Statistics (ISTAT)[5]. Specific mortality data for the years 2003, 2006 and 2007 were used to validate expected mortality projections, as ISTAT had yet to publish data for 2004-2005. Relative survival estimates were calculated by means of parametric cure models of the Weibull type at the level of macro area, using data from cancer registries included in the EUROCARE-4 study for the period 1985-2002[6]. The survival estimates for the southern macro area were assigned to Sardinia for all cancer sites. The survival time trend after 2002 was assumed to have the same tendency as that estimated for the 1985-2002 period for all cancers except prostate cancer, where the survival was assumed to be constant from 2005 onwards.

For cervix cancer, prostate cancer and melanoma, additional procedures were applied to account for problems specifically related to these cancers. Cervical cancer estimates were only feasible from the year 1980, after the adoption in mortality statistics of the ninth revision of the International Classification of Diseases (ICD-9), which allowed to make a distinction between cancer of the cervix, corpus uteri, or uterus not otherwise specified (NOS). Unfortunately, the official mortality statistics for cervical cancer are undersized due to the misclassification of a great proportion of cervical and corpus uteri cancers into uterus NOS. For this reason, the estimates for this site were performed after adjustment of mortality data for such misclassification, using the method proposed by Capocaccia *et al.*[7], and they were carried out only up to age 94 years. Furthermore, only limited-duration prevalence at 15 years is herein reported, as complete prevalence would have been not reliable.

For prostate cancer, a specific procedure was used to capture recent rapid variations of time trends, as suggested by the most recent cancer registries' data[8]. Mortality estimation up to the year 2010 was preliminarily performed by means of the PIAMOD method[9] so as to complete the missing mortality time series in the years 2004 and 2005[5], and to base incidence estimates on mortality data at least 5 years after the suspected incidence turning point. This longer mortality time series was then used as input for the MIAMOD method.

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

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

Results

The estimated values of the incidence, mortality and prevalence indicators in the year 2012 are presented in Tables 2A and 2B for men and women separately. Differently from most Italian regions, colon and rectum were the most frequently diagnosed cancer sites in Sardinia for men, with 833 estimated new cases in 2012, followed by lung (744 cases) and prostate (667 cases). A lower incidence was estimated for stomach cancer and melanoma, with 140 and 74 new cases, respectively. Mortality rates were highest – and very close to the incidence rates – for lung cancer (606 deaths), due to its very poor prognosis. Colorectal cancer was the second cause of death (318 deaths), followed by prostate cancer (198 deaths), stomach cancer (98 deaths) and melanoma, with only 12 expected deaths. In women, breast was by far the most frequent cancer site, both regarding incidence (1,512 new cases) and mortality (295 deaths), followed by colon-rectum (493 cases and 201 deaths), lung (205 cases and 167 deaths), melanoma (106 cases and 15 deaths), stomach (82 cases and 61 deaths), and uterine cervix (36 cases and

19 deaths). Breast was also the cancer site with the highest prevalence (15,180 cases), while for colorectal cancer a total of about 7,300 prevalent cases was estimated in both sexes. The other cancer sites presented a much lower prevalence, from 2142 cases for lung cancer to 875 cases for stomach cancer.

The time trends of the 3 indicators over the period 1970-2015 are shown in Figures 1 to 6. They present age-standardized incidence rates in men (Figure 1) and women (Figure 2), age-standardized mortality rates in men (Figure 3) and women (Figure 4), and crude prevalence in men (Figure 5) and women (Figure 6). All the rates are provided for 100,000 population/year, while prevalence is expressed as the proportion per 100,000 persons alive in the population. The results will be described below, grouped by cancer site.

Stomach

The trends in incidence and mortality for stomach cancer show a progressive reduction in both sexes. The incidence is estimated to steadily decrease in the period 1970-2015 from 29 to 11 in men and from 17 to 4 in women. In the same period the mortality will drop from 26 to 7 and from 15 to 3, respectively, in men and women. Conversely, the stomach cancer prevalence is estimated to increase in both genders: slowly in women (from 30 per 100,000 in 1970 to 38 in 2015) and more rapidly in men (from 26 per 100,000 in 1970 to 76 in 2015).

Colon and rectum

For colorectal cancer, incidence and mortality show different trends in the 2 sexes. In men, a linear increase in incidence from 16 to 74 was estimated in the period 1970-2015, while the observed mortality increase tended to level off after the year 2000, and the projected values reach an almost constant level, about 26 in 2015. In women, both incidence and mortality show an initial phase of rising rates, with a peak in 1999 (33 per 100,000) and 1994 (17 per 100,000), respectively, and a successive drop until the end of the considered period. In relative terms the decrease was more marked for mortality (-40% from 2000 to 2015) than for incidence (-12% in the same period). The crude prevalence proportion is estimated to rise quickly from 1970 to 2015 for both sexes: from 19 to 628 per 100,000 in men and from 27 to 428 per 100,000 in women.

Lung

Lung cancer presents very different gender-specific patterns, and the incidence and mortality trends are very close to each other due to the low survival. In men, these rates increased up to a maximum 81 for incidence and 71 for mortality and steeply decreased starting 1995, returning by 2015 to values similar to those at the end of the 1980s. Conversely, both the incidence and mortality trends are rising in women, from 6 to 15 and from 5 to 12, respectively. The prevalence is estimated to still rise in men (up to 234 in 2015), while for women it remains relatively low (66 in 2015) because of the relatively recent spread of this cancer among the female population.

Skin melanoma

The estimated incidence rates of melanoma present a steep and progressive increase in both sexes. The age-standardized incidence rates were similar between men and women until the late 1990s, while in subsequent years higher incidence rates were estimated in women than men. In 2015 the female incidence rate is estimated to be more than 1.5 times greater than the male incidence rate (12.6 *vs* 7.8). The age-standardized mortality rates are quite low due to the relatively high survival rate of melanoma patients. The male estimates show a rapid rise between 1970 and the late 1980s, a lesser increase during the 1990s, and a slight decrease from 2000 onwards. By contrast, the female mortality trend appears to be increasing steadily: from 0.4 per 100,000 in 1970 to a projected value of 1.3 per 100,000 in 2015. The prevalence proportions of melanoma patients are estimated to rise exponentially for both sexes, reaching higher projected values in 2015 for women (155/100,000) than for men (103/100,000).

Breast

The breast is the most common cancer site in women. The incidence estimates for breast cancer show a sharply increasing trend for the whole considered period (from 28 per 100,000 in 1970 to 136 in 2015). By contrast, the mortality estimates, after an initial ascending phase from 18 per 100,000 in 1970 to about 29 per 100,000 in the first half of the 1990s, subsequently decreased to reach 19 per 100,000 in 2015. The prevalence proportions are steeply increasing and are estimated to reach an extremely high value in 2015 (2,170 per 100,000).

Cervix uteri

During the study period 1980-2015, all the epidemiological indicators for cervical cancer were estimated to decline consistently. The age-standardized incidence rate drops by a 3-fold ratio (from 9 to 3), while the age-standardized mortality decreases by a 4-fold ratio (from 4.9 to 1.3). Cervical cancer is the only malignancy, among those considered, showing a decreasing prevalence. The 15-year limited-duration prevalence is forecast to be about 36 per 100,000 in the year 2015.

Prostate

The prostate cancer incidence was estimated to increase from 1970, and particularly sharply from 1990,

until 2003, when the age-standardized incidence rates reached their maximum of 64 per 100,000. Under the hypotheses presented in the Methods section, the incidence estimates show a subsequent reduction, down to 44 in 2015. The age-standardized mortality rates show a slight rise until 2000 followed by a tendency to decline, from 20 per 100,000 to 13 in 2015, approaching the rates observed in 1970. The prevalence is expected to rise sharply in the forthcoming years, up to 638 per 100,000 in 2015.

Discussion

In this paper we present the most recent estimates of cancer incidence, mortality and prevalence of the 7 major cancer sites in the Sardinian population. The estimates and projections were subsequently compared with the available observed data. For this purpose the Sassari cancer registry was chosen because it had data available from 1992 to 2006, whereas the Nuoro registry data started in 2003. The comparisons indicated good agreement between the age-standardized incidence rates estimated in Sardinia and those observed in the Sassari registry, which, however, are not necessarily representative of the entire region. The only exception was melanoma of the skin, for which the most recently observed values appeared to be substantially lower than the corresponding model-based estimates, particularly in women. As a consequence, our regional projections to the year 2015 are probably overestimated.

The incidence trends of cancer have changed over time, and the many reported patterns can be compared with known variations in the prevalence of risk factors. The reduction in the incidence and mortality of gastric cancer is a general phenomenon that has been observed in most Western countries. It is mostly related to the improved preservation and cooking of foods and to improved food quality. A possible contribution to the declining stomach cancer rates may have come from the use of new diagnostic techniques for early diagnosis and the eradication of *Helicobacter pylori* infection, a known risk factor for this cancer[10].

Colorectal cancer showed a lower incidence than the national average in women throughout the considered period, while in men the estimated incidence rates increased much more rapidly than the national estimates so that, starting from 2012, the regional Sardinian rates will surpass the national data. The female mortality rates were lower than the Italian rates in the period 1970-2015, while the male mortality rates were higher than the national estimates from 2007 onwards. The trend of this cancer is hardly influenced by organized screening (which is starting only now in some local health units) or by opportunistic screening, which is not widespread among the general population. Colorectal cancer is strongly correlated with a number of risk factors including poor diet, physical inactivity, excess weight and alcohol consumption. Only 14% of the Sardinian population take the recommended servings (5 a day) of fruit and vegetables. This percentage is, however, higher than the national average (10%) and is higher in women than men (16% and 12%, respectively)[11-13]. According to the ISTAT multipurpose survey of 2010, physical inactivity affects 35% of the population and the percentage is lower than the national average (40%), while excess weight affects 46% of the population and this value is equal to the national average[14,15]. In 2011 in Sardinia the prevalence of wine consumers aged more than 11 years was 49%, which is below the national level (53%)[15].

The lung cancer incidence is decreasing in men and rising in women; it is closely related to trends in cigarette smoking. In 2010 the Sardinian prevalence of smokers among those aged 15 years or more was 26.7% in men and 16.6% in women. The time trend of smoking prevalence is comparable to the national trend and is decreasing in the male population and increasing in the female population[2].

The breast cancer incidence is estimated to increase during the study period, while the mortality, after reaching a peak in 1993, is rapidly decreasing. Organized mammography screening was started in 2006 in the northern Sardinia health unit; other local health units followed. The data of the report of the National Screening Observatory[16] show an adherence to the screening program in 2007 equal to 43%, compared with 61% in northern Italy. However, opportunistic screening is sufficiently rooted in Sardinia. In spite of the controversy about its effectiveness and the problem of overdiagnosis[16], screening, whether organized or opportunistic, has played a major role in reducing mortality and cases of advanced disease. Secondary prevention is therefore very important in the fight against this cancer, although primary prevention campaigns to reduce its determinants (overweight, physical inactivity, unhealthy diet) may lead to a further reduction of the number of cases[17-19]. Other risk factors such as age, family history, and inheritance of mutated tumor suppressor genes (BRCA1 and BRCA2)[20] have not been evaluated.

Regarding cervical cancer, the declining incidence and mortality trends positively reflect the effect of opportunistic screening, which is widespread in Sardinia. Screening has led to subclinical diagnosis of cancer and to diagnosis of cytological precursor lesions amenable to appropriate treatment[21]. The introduction of the practice of vaccination against HPV in public health services could lead to the eradication of this cancer in the next years.

Prostate cancer in Sardinia shows incidence and mortality trends common to all high-income countries, with a strong increase in incidence during the 1990s peaking in the early 2000s, and a subsequent decrease from the year 2005. The increase in incidence is largely attributable to the introduction of opportunistic

screening with the PSA test, which has led to a high proportion of overdiagnoses (according to estimates, more than 50% of the total diagnoses also for middle-aged men)[22]. The main determinants of prostate cancer are age, followed by familiarity, race, genetic factors (mutations in BRCA1 and BRCA2 result in a cumulative risk of 8%)[20,22-24], a diet rich in saturated fat[25,26], and low blood levels of vitamin D[27].

The epidemiology of the major cancer types in Sardinia indicates a general decrease in mortality – with the exception of lung cancer in women – but different site- and sex-specific incidence trends. The prevalence is, however, steeply increasing for all the considered cancers (the only exception being cancer of the uterine cervix). This points to the need of more strongly supporting evidence-based prevention campaigns focused on contrasting female smoking, unhealthy nutrition, and sun exposure. Reinforcing organized screening activities could additionally contribute to limit the impact of the increasing trends of breast and colorectal cancer.

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

		Population	Population ≥65 years of age %	Coverage %	First year of incidence
Region	Sardinia	1,675,411	19.4	43	1992
Registry	Sassari-Olbia	495,096	18.9	Province	1992
	Nuoro-Ogliastra	218,642	20.5	Province	2003

Table 2A – Estimated incidence, mortality and prevalence by cancer site for the year 2012 in Sardinia. 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

	Incidence			Mortality			Prevalence	
Cancer site	Number of cases	Crude rate	Age-std rate	Number of deaths	Crude rate	Age-std rate	Number of cases	Crude proportion
Prostate	667	81.7	49.5	198	24.3	13.9	4,845	593.4
Stomach	140	17.9	12.0	98	12.5	8.2	558	71.0
Colon-rectum	833	106.0	70.2	318	40.4	26.1	4,142	527.2
Lung	744	94.6	63.5	606	77.1	50.8	1,663	211.5
Melanoma	74	9.4	7.3	12	1.5	1.1	677	86.2

Table 2B – Estimated incidence, mortality and prevalence by cancer site for the year 2012 in Sardinia. 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

	Incidence			Mortality			Prevalence	
Cancer site	Number of cases	Crude rate	Age-std rate	Number of deaths	Crude rate	Age-std rate	Number of cases	Crude proportion
Breast	1,512	183.4	127.2	295	35.8	20.7	15,180	1,842.1
Stomach	82	10.0	4.9	61	7.5	3.5	317	38.4
Colon-rectum	493	59.9	29.9	201	24.4	11.5	3,211	389.6
Lung	205	24.9	14.5	167	20.2	11.4	479	58.1
Melanoma	106	12.9	11.2	15	1.9	1.2	1,033	125.4
Cervix	36	4.4	3.1	19	2.4	1.4	315*	38.3*

*Limited-duration prevalence at 15 years.

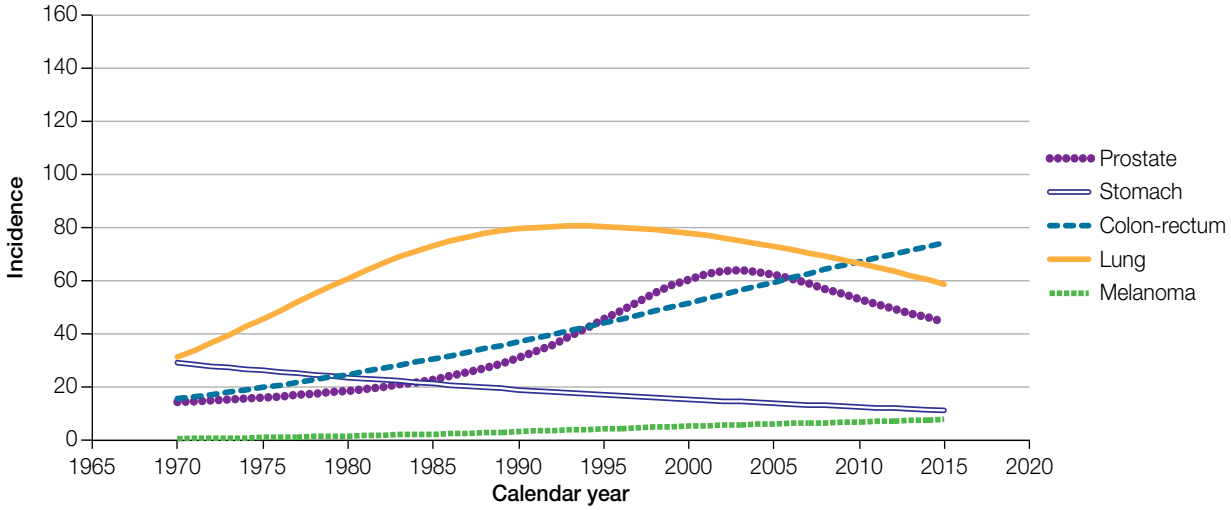


Figure 1 - Incidence estimates by cancer site in Sardinia in the period 1970-2015. Age-standardized rates (European population) per 100,000 person-years. Age 0-99 years, men.

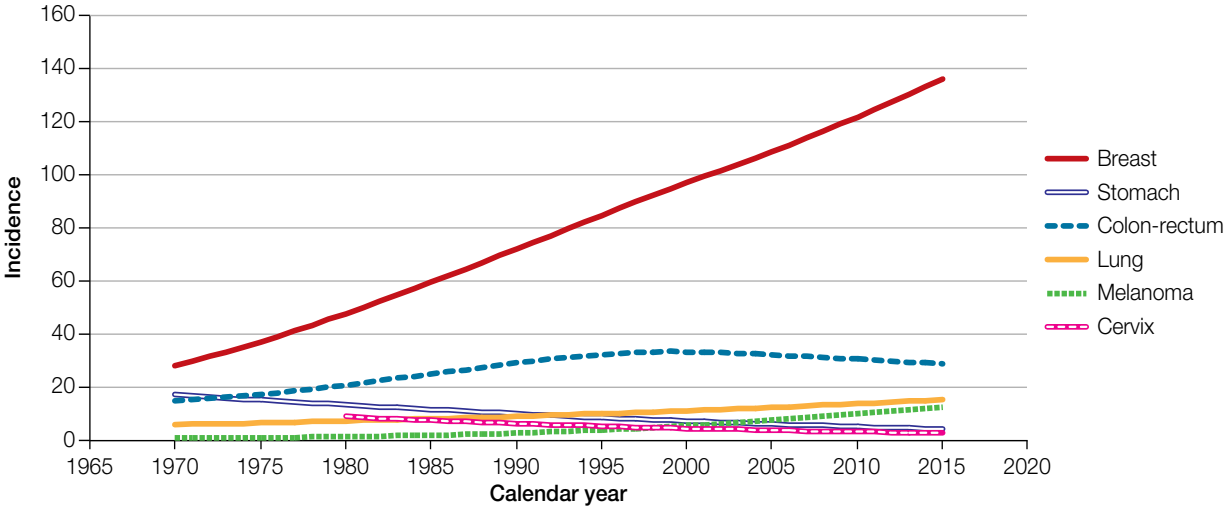


Figure 2 - Incidence estimates by cancer site in Sardinia in the period 1970-2015. Age-standardized rates (European population) per 100,000 person-years. Age 0-99 years, women.

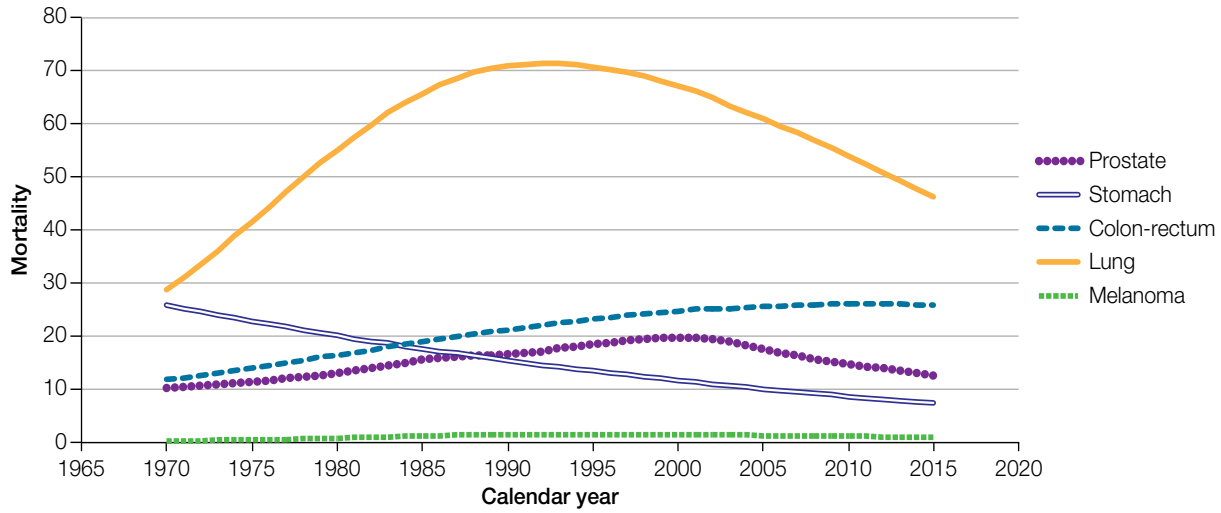


Figure 3 - Mortality estimates by cancer site in Sardinia in the period 1970-2015. Age-standardized rates (European population) per 100,000 person-years. Age 0-99 years, men.

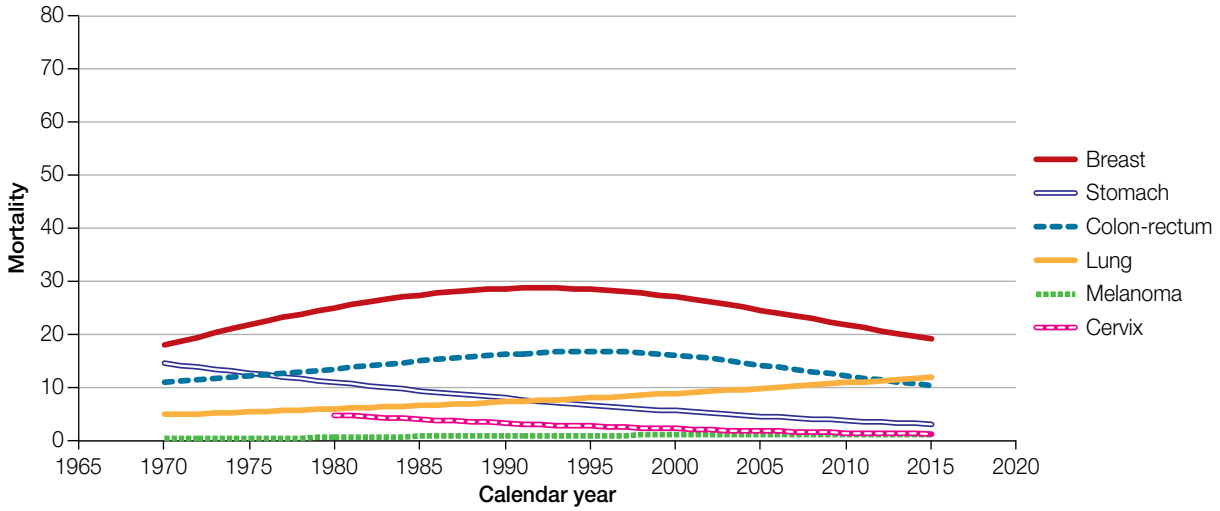


Figure 4 - Mortality estimates by cancer site in Sardinia in the period 1970-2015. Age-standardized rates (European population) per 100,000 person-years. Age 0-99 years, women.

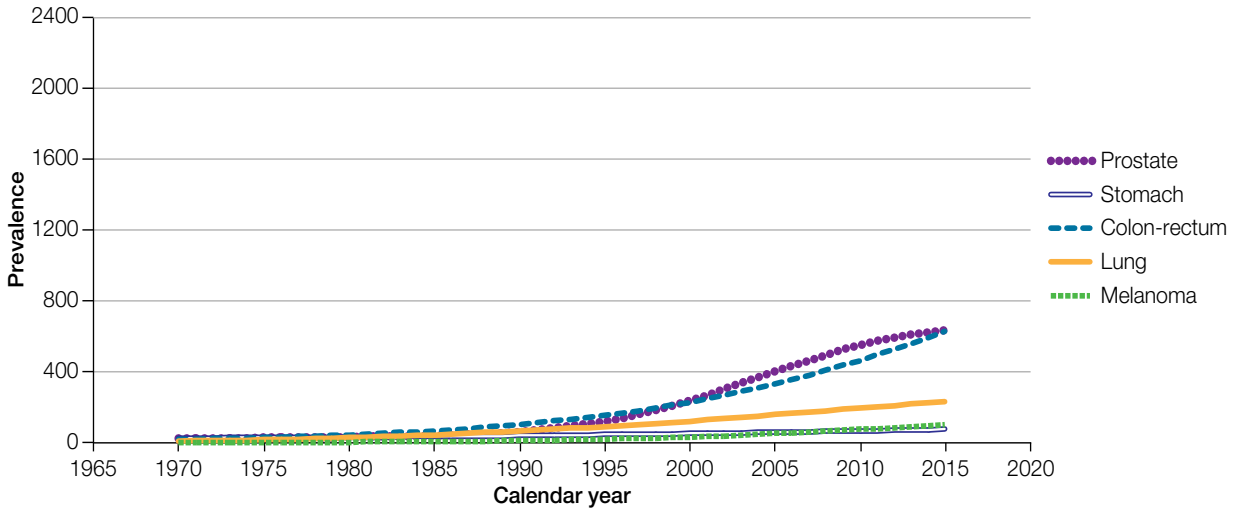
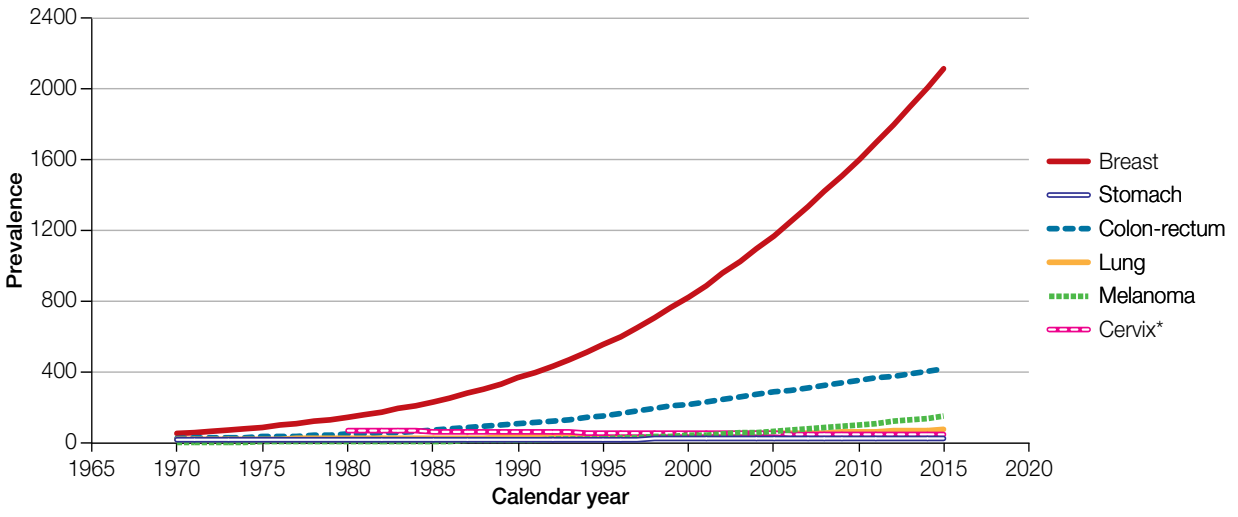


Figure 5 - Prevalence estimates by cancer site in Sardinia in the period 1970-2015. Crude proportion per 100,000 persons. Age 0-99 years, men.



*limited-duration prevalence at 15 years

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

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