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Estimates of cancer burden in Marche

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ABSTRACT

Aims and background. The aim of this paper is to provide estimates of the incidence, mortality and prevalence of seven major cancers in the Marche region for the period 1970-2015.

Methods. The MIAMOD method, a statistical back-calculation approach, was applied to derive incidence and prevalence figures from mortality and relative survival data. Published data from the Italian cancer registries were used as the basis for survival modeling.

Results. Colorectal, breast and prostate cancer were the most frequent cancers in 2012, with 1,563, 1,215 and 1,191 estimated incident cases, and leading to 539, 224 and 228 deaths, respectively. Age-standardized rates were estimated to decrease for stomach and cervical cancer and to increase for skin melanoma and female lung cancer. In men, the lung cancer incidence rates reached their maximum level during the late 1980s and decreased thereafter. The colorectal cancer trend showed an initially increasing pattern, followed by a decrease in the last decade, both for men and women. The estimated incidence rates of prostate cancer presented a very steep rise in the period 1985-2002 and then remained stable at the high levels reached in 2003. The largest increases in prevalence were for breast, colorectal and prostate cancer, for which 17,098, 11,844 and 9,269 cases were estimated, respectively, in 2012.

Conclusion. This paper provides a description of the burden of the major cancers in the Marche region until 2015. The estimates were fairly consistent with previously published data by the Macerata province cancer registry. The MIAMOD method provides a picture of the impressive increase in the prevalence of breast cancer and prostate cancer over the period studied, thereby allowing to foresee an increasing demand for cancer care services as one of the major challenges for the regional health care system.

Introduction

The Marche is a medium-size region of central Italy with a population of about 1.5 million. In 2011, the percent ratio between the number of persons older than 65 years and those younger than 15 years, known as the aging index, was equal to 168%, showing a regional population older than the national one (144% in Italy). In the same year the regional old-age dependency index (the percent ratio between the population older than 65 years and the active population aged 15-64 years) was 35% (31% in Italy). Per capita gross domestic product (25,150 euro¹) and per capita health expenditure were about the same as those registered at the national level (25,032 euro).

Neoplastic diseases are the second cause of death among both men and women in the Marche region². Regional cancer care is supported by 15 hospitals with medical oncology services³ and 21 non-specialist-cure centers. A total of 12 beds per 1,000 persons are available in the regional medical oncology services, similar to the national mean of 11 beds per 1,000 persons⁴.

Key words: cancer, incidence, prevalence, mortality, Marche, estimates.

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Breast and cervical cancer screening programs started in 2000 in the whole region, while colorectal cancer screening started in 2011⁵.

The aim of this paper is to describe the time trends of incidence, mortality and prevalence for the major cancer sites (lung, stomach, colon-rectum, breast, prostate, cervix and skin melanoma) in the Marche region and to estimate these epidemiological indicators up to 2015.

Material and methods

Mortality data for all cancers, general mortality and population data by age, calendar year and geographical region for the periods 1970-2003 and 2006-2007 were obtained from the Italian National Institute of Statistics (ISTAT)⁶. Relative survival data for the considered cancers for the period of diagnosis 1985-2002 were obtained from the EUROCARE-4 study⁷. They refer to the populations covered by 21 cancer registries in Italy jointly covering about 25% of the national population.

The MIAMOD method⁸⁻¹⁰ was used for the 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 from mortality and survival data. The method relies on the mathematical relationships between mortality, prevalence, incidence and survival. The model estimates presented in this paper are 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)¹¹. The subsequent years, i.e. 2003, 2006 and 2007 (data for 2004-2005 were not yet released 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. To obtain stable survival estimates, these were carried out by grouping the registries into 4 geographical macro areas: northwest, northeast, center and south + islands. Geographical area and patients' age were considered as categorical covariates in the survival model. The way of considering the year of diagnosis (continuous or categorical) and the choice of having a unique term for period and risk or various terms for each geographical area depended on the tumors and the sex¹⁰. The survival estimates for central Italy (including the registries of Tuscany, Marche, Umbria and Lazio) were assigned to Marche.

The survival time trend after the year of diagnosis 2002 was assumed to have the same tendency as that estimated over the observation period of diagnosis 1985-2002 for all cancers except prostate cancer, where 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 melanoma, additional procedures were applied to account for specific problems related to these sites. For cervical cancer a methodology^{12,13} was used to adjust the mortality data provided by the official statistics, as these were flawed by misclassification with uterus not otherwise specified (NOS). This methodology could be applied from 1980 onwards because before that year the ICD-8 classification, which did not distinguish uterus NOS, was used in the ISTAT statistics. The corrected mortality data were used as input for incidence and prevalence estimates by the MIAMOD method. Estimates for cervical cancer 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 trends¹⁴, more up-to-date mortality data were used in order to capture recent variations which could not be modeled with data up to 2002. Since mortality data for 2004-2005 were missing, mortality estimates with projections up to 2010 were preliminarily performed by means of the PIAMOD method¹⁵. The modeled mortality rates were then used as input for the MIAMOD method.

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

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

Results

Two cancer registries are active in the Marche region: the Macerata Cancer Registry, which provides incidence data since 1991 and covers the whole province of Macerata (about 325,000 people, 21% of the regional population), and the Marche Childhood Cancer Registry, which has been operating since 1996 and covers the whole regional population aged 0-14 years (1996-1997) and 0-19 years (since 1998)¹⁶. Table 1 reports the main descriptive data of the 2 active registries, 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.

The number of cases and both the crude and age-standardized incidence and mortality rates and prevalence proportions estimated in Marche for 2012 are presented in Tables 2A and 2B for men and women, respectively.

Prostate and colon-rectum were the most frequently diagnosed cancer sites among men, with 1,191 and 854 estimated new cases, respectively, and preceding lung (592), stomach (317) and skin melanoma (230). The most frequent causes of cancer death were lung cancer (518 deaths expected in 2012) and colorectal cancer (293), with crude mortality rates of 74 and 42 deaths per 100,000 persons/year. The most frequent female cancer site was breast, with the highest estimated number of new cases (1,215), followed by colon and rectum (709). The incident cases for lung cancer, stomach cancer, melanoma and cancer of the cervix uteri were considerably lower. Colorectal and breast cancer were also the 2 sites with the highest female mortality rates, with 246 and 224 expected deaths and crude mortality rates of 33 and 31 per 100,000 in 2012, respectively.

The highest prevalence was estimated for breast cancer in women and prostate cancer in men. The Marche region was estimated to have in 2012 over 17,000 women with a previous diagnosis of breast cancer, over 11,000 people with colorectal cancer, and about 9,300 men with prostate cancer.

The time trends of the age-standardized incidence and mortality rates and crude prevalence proportions over the period 1970-2015 are shown in Figures 1 to 6 for both sexes. The results will be described below, grouped by cancer site.

Stomach

Consistent with estimates in other Italian regions, stomach cancer presented decreasing standardized annual incidence rates in men, which during the study period dropped from 71 to 26 estimated cases per 100,000. The female incidence rates followed the same pattern at about half of the male level. Mortality behaved similarly, starting in men at 61 per 100,000 in 1970 and declining to 14 per 100,000 in 2015. The corresponding values for women were 30 and 7.4. While the stomach cancer incidence and mortality were estimated to be steadily decreasing, the prevalence increased in both sexes, especially among males, more than doubling in 2015 with respect to 1970 (from 116 to 246 per 100,000). Women faced a smaller, almost negligible increase (from 142 to 162).

Colon and rectum

The estimated trends of colorectal cancer incidence were similar in men and women. In both sexes an in-

crease was estimated from 1970 (age-standardized incidence rates of 35 per 100,000 for men and 28 for women) until the mid 1990s (71 in men and 46 in women), and a final, slow stabilization around the levels of 65 in men and 41 in women. The age-standardized mortality rates followed an increasing pattern until the end of the 1980s and a subsequent decrease, with higher levels in men (24 per 100,000 in 1970 compared to 19 in women, and 20 versus 12 in 2015). These trends resulted in a higher prevalence in men: in 2015 956 prevalent cases per 100,000 population were estimated among men versus 815 per 100,000 in women.

Lung

The lung cancer incidence estimates in men showed a turning point in the late 1980s and a subsequent substantial reduction, from 77 per 100,000 in 1990 to 42 in 2015. By contrast, in women we estimated a continuous and more than 3-fold increase in age-standardized rates (from 5 to 19 per 100,000 in 2015). Mortality followed a similar pattern to incidence: the female age-standardized mortality rate increased from 5 per 100,000 in 1970 to 14 per 100,000 in 2015, while the male mortality increased from 32 to 67 per 100,000 in 1989 and then decreased to 35 per 100,000. Prevalence rose for both sexes, from 5 to 105 estimated cases per 100,000 in 2015 for women and from 34 to 209 for men.

Skin melanoma

The incidence of skin melanoma presented very similar, increasing trends in men and women, with a slightly more marked increase among women. The estimated age-standardized incidence rates increased during the period 1970-2015 from 4 to 34 per 100,000 in women and from 2 to 26 per 100,000 in men. In comparison, the rise in mortality was less steep: from 0.7 to 1.4 per 100,000 in women, and from 1.7 to 2.4 per 100,000 in men. The female prevalence was estimated to rise from 33 to 539 and the male prevalence from 8 to 343 per 100,000.

Breast

The age-standardized incidence rates for breast cancer were estimated to rise with a linear trend from 1970 until the late 1990s and then to remain stable at a plateau rate of 105 cases per 100,000 during the period 2002-2010. After this period, a slow decrease is expected to about 100 per 100,000 by 2015. The age-standardized mortality rates rose from 21 per 100,000 in 1970 to 27 per 100,000 in 1988 and then decreased to 13 per 100,000 in 2015. The estimated prevalence increased rapidly, from 143 to 2,541 per 100,000 women during the considered period.

Cervix uteri

For cervical cancer, we estimated a generalized continuous improvement in all indicators over time. The age-standardized incidence rates decreased from 12 to 5 per 100,000, and mortality from 6 to 1 per 100,000. Cervix is the only cancer site among those considered in this analysis with decreasing prevalence, which was estimated to drop from 138 to 59 cases per 100,000 women living in the Marche region.

Prostate

The incidence of prostate cancer has shown a steep increase in all Italian regions during the 1990s. According to our estimates the age-standardized rates will increase from 25 per 100,000 in 1970 to about 90 per 100,000 in 2015. After the period 1984-1998, in which the prostate cancer mortality remained at about 20 deaths per 100,000, the mortality rates are projected to decrease, returning by 2015 to the level observed in 1970, i.e. about 14 per 100,000. Prevalence is estimated to have increased dramatically, from 70 in 1970 to 1,341 prevalent cases per 100,000 men in 2015.

Discussion

The present paper illustrates the estimated patterns of new cases, deaths and prevalence of the major cancers in the Marche region. The incidence rates for all studied cancers declined or stabilized, with the only exception of skin melanoma and lung cancer in women.

The incidence estimates were compared for validation purposes with the observed incidence rates collected by the Macerata province cancer registry. The comparison between indicators referring to the whole region and those collected in a single province may be partially misleading due to possible intraregional heterogeneity in socioeconomic and environmental factors. Nonetheless, the estimated and observed rates are substantially consistent (data not shown).

The estimated indicators seem also to be coherent with what is known about risk factor trends, even in the presence of gender-specific patterns. Smoke is a major risk factor for cancers of the lung and, to a lesser extent, stomach and cervix. The data of the "Heart Project" conducted by the Italian National Institute of Health (ISS) show a decreasing prevalence of smokers in the regional population¹⁷, especially among men (from 29% to 23% between 2000 and 2010), as well as decreasing exposure to passive smoke. The prevalence of smokers aged 15 years or more according to the data of 2011¹⁸ was similar to the national estimate in men (28.2 *vs* 28.7), whereas in women the prevalence was slightly higher in Marche than in Italy as a whole (16.8% *vs*

15.4%). Particular attention should be paid to the fact that the smoking prevalence in the Marche region seems to be higher among people under 34 years of age¹⁹.

Diet and obesity are 2 other important risk factors, particularly for digestive tract and breast cancer. The proportion of overweight people is higher in Marche^{18,20} than in the overall Italian population, but only half of the overweight people stated they had received general dietary advice from their general practitioner as a preventive measure²¹.

Colorectal, breast, cervical and male lung cancers benefit from the spread of activities aimed at early diagnosis and from prevention campaigns and regulation.

Breast cancer screening started in Marche in 2000 and reached a percentage of invited women aged 50-69 ranging between 73% and 84% in the period 2007-2010. The participation rate was about 50%, with an additional substantial proportion of women (22%) having mammograms outside the screening program²¹.

Non-organized screening plays an important role also in cervical cancer: it involved 24% of women aged 25 to 64 years compared with a coverage of 50% by organized programs during the period 2006-2009²¹.

Colorectal screening started later, in 2011, and attendance has been low⁵. It cannot therefore be supposed to have played a role in the estimated decrease in incidence of this cancer. A further review will be necessary to understand the joint effect of colorectal screening and improvement of therapeutic effectiveness on the future trends of all indicators related to this cancer.

The prostate cancer incidence trend reflected the widespread use of PSA testing, even if no organized screening was in place. The decrease in prostate cancer mortality since 1999 seems to suggest some positive effects of the spread of PSA testing. We cannot determine to what extent true risk factors including diet have contributed to such a trend.

The decreasing incidence and mortality trends of cervical cancer are reflected in its prevalence, with an estimated 91 cases per 100,000 women in 2015 compared with the initial level of 295 per 100,000 in 1980. Similar incidence and mortality trends were estimated for stomach cancer and male lung cancer. However, while the lung cancer prevalence was estimated to increase 3-fold (from 35 to 109 prevalent cases per 100,000 men), the stomach cancer prevalence estimates remained stable in men (from 124 to 133 prevalent cases per 100,000 men) and almost halved in women (from 124 to 71 prevalent cases per 100,000 women). In the next years particular attention should be paid to the growth of prevalent cases in breast, prostate and colorectal cancers and in skin melanoma. The expected increase in prevalence rates, jointly with population aging, will produce an important burden for the health care system.

Table 1 - Marche population, proportion of the elderly population and cancer registries with their coverage and beginning of activity

Registry	Population covered	Population count by 2011	Population ≥65 years of age %	Regional coverage %	First year of incidence
Macerata cancer registry	Macerata province	325,362	23%	21%	1991
Childhood cancer registry of the Marche region	Marche regional population	279,046	-	100%	1996

Table 2A – Estimated incidence, mortality and prevalence by cancer site for the year 2012 in Marche. 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	1,191	155.1	88.3	228	29.6	14.0	9,269	1,206.6
Stomach	317	45.4	25.6	207	29.6	15.9	1,686	241.5
Colon-rectum	854	122.3	67.2	293	41.9	21.7	6,215	889.8
Lung	592	84.7	46.8	518	74.1	39.9	1,492	213.6
Melanoma	230	32.9	23.6	28	4.0	2.4	1,936	277.4

Table 2B – Estimated incidence, mortality and prevalence by cancer site for the year 2012 in Marche. 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	1,215	165.1	104.0	224	30.5	14.5	17,098	2,322.0
Stomach	212	28.8	12.9	139	18.8	7.7	1,201	163.1
Colon-rectum	709	96.2	41.8	246	33.4	13.1	5,629	764.4
Lung	266	36.2	18.1	200	27.1	12.8	651	88.4
Melanoma	287	39.0	30.9	21	2.8	1.6	3,413	463.7
Cervix	25	6.2	4.6	11	2.6	1.5	253*	61.5*

*Limited-duration prevalence at 15 years.

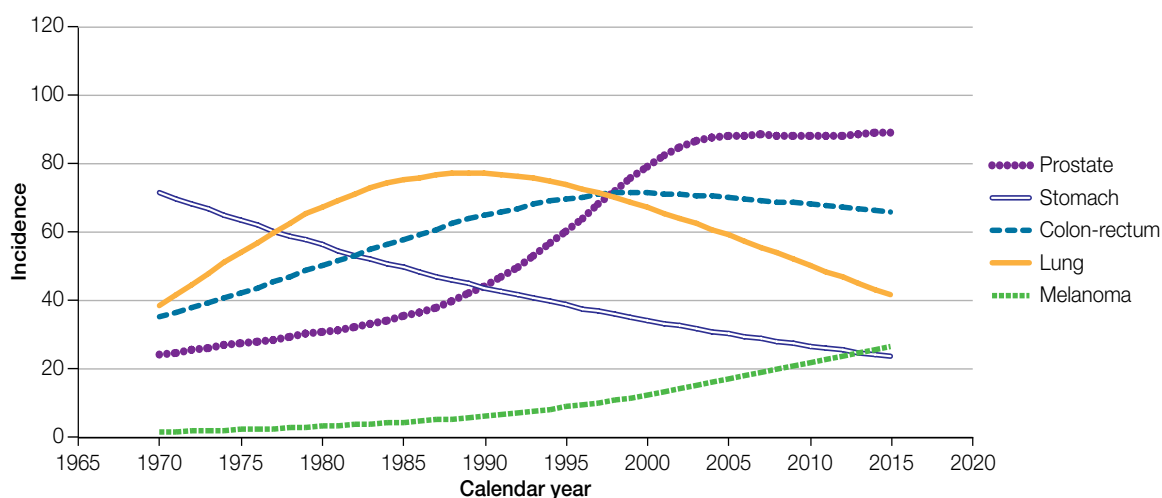


Figure 1 - Incidence estimates by cancer site in Marche in the period 1970-2015. Age-standardized rates (European population) per 100,000 person-years. Age 0-99 years, men.

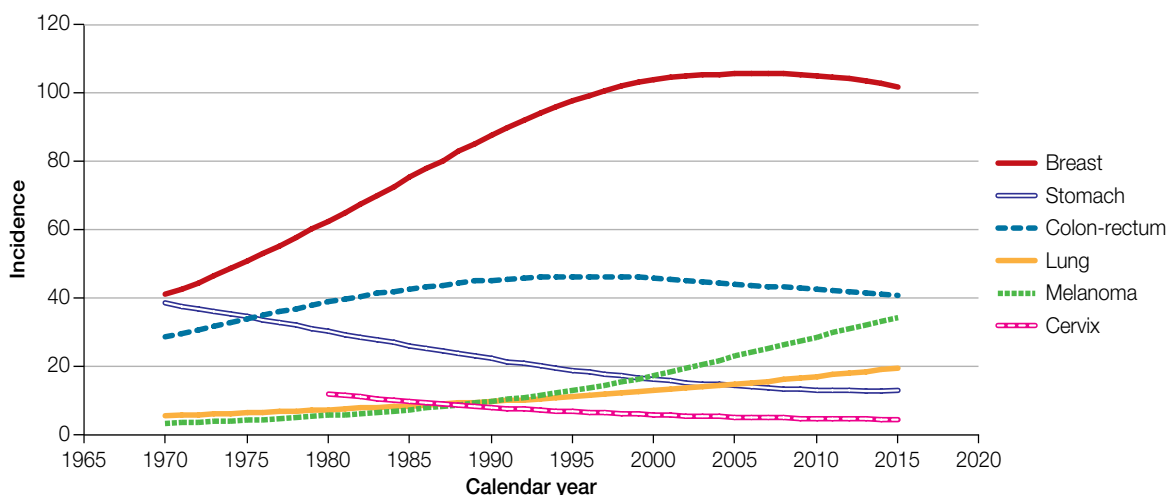


Figure 2 - Incidence estimates by cancer site in Marche in the period 1970-2015. Age-standardized rates (European population) per 100,000 person-years. Age 0-99 years, women.

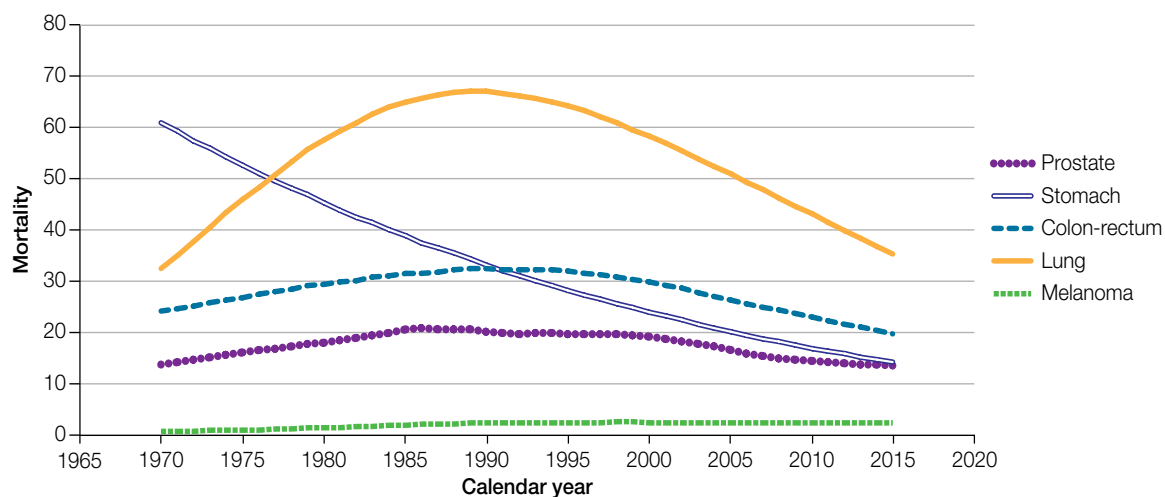


Figure 3 - Mortality estimates by cancer site in Marche in the period 1970-2015. Age-standardized rates (European population) per 100,000 person-years. Age 0-99 years, men.

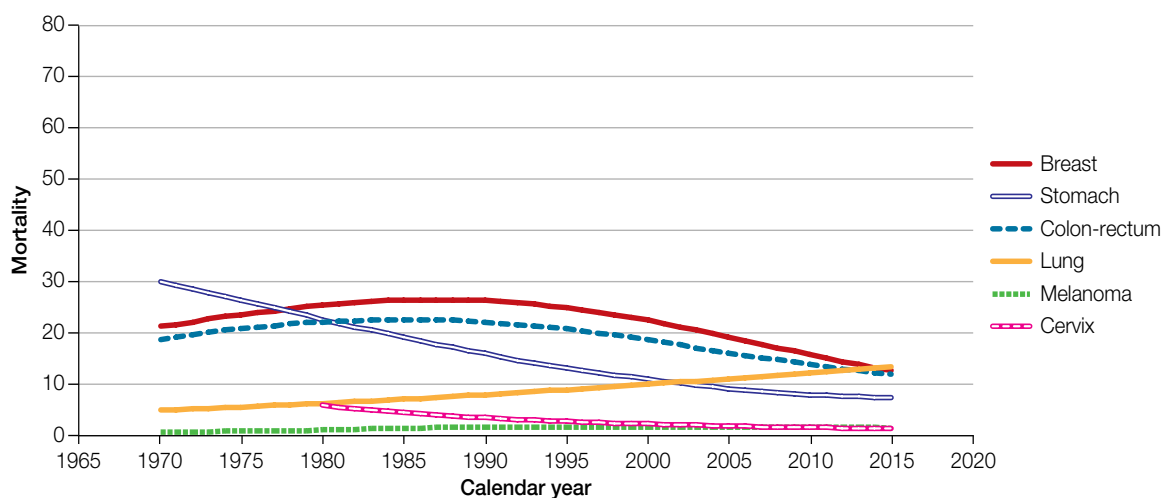


Figure 4 - Mortality estimates by cancer site in Marche in the period 1970-2015. Age-standardized rates (European population) per 100,000 person-years. Age 0-99 years, women.

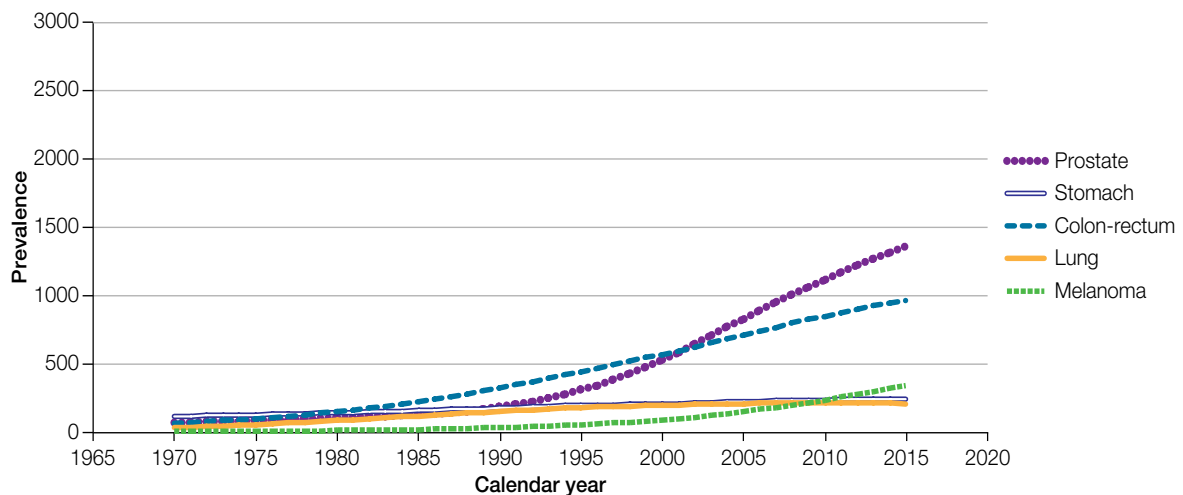
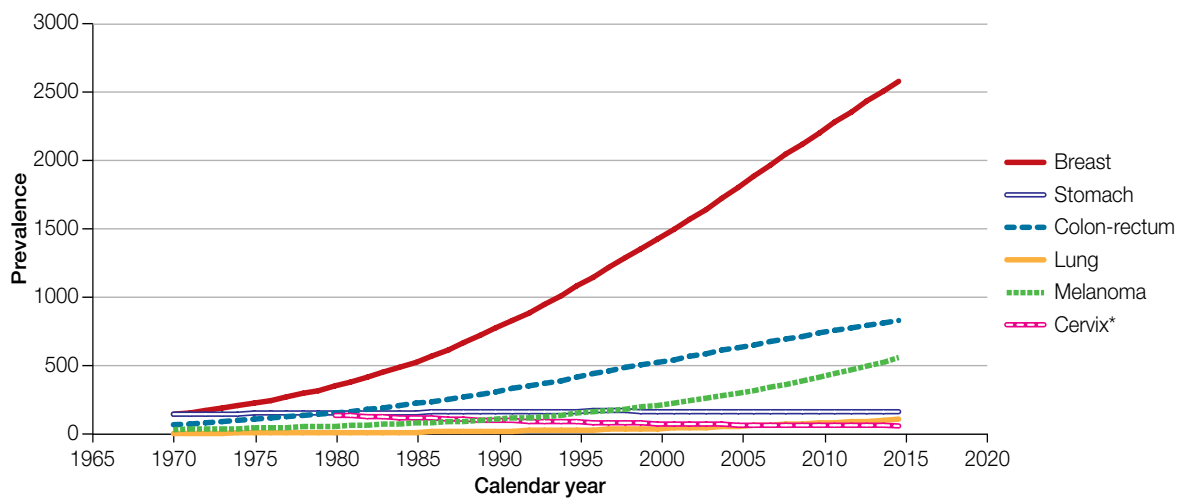


Figure 5 - Prevalence estimates by cancer site in Marche in the period 1970-2015. Crude proportion per 100,000 persons. Age 0-99 years, men.



*limited-duration prevalence at 15 years.

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

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