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Estimates of cancer burden in Umbria

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ABSTRACT

Aims and background. Model-based estimates and projections of epidemiological indicators related to cancer are important tools to support public health policies and planning. The aim of the present study is to produce projections of cancer incidence, mortality and prevalence for the Umbria region (900,000 inhabitants) in central Italy.

Methods. The estimations 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. Published data from the Italian cancer registries were modeled in order to estimate regional cancer survival. Estimated incidence rates were validated with observed incidence rates obtained from the Umbria regional cancer registry.

Results. The most frequent cancer sites estimated were colon-rectum, prostate and breast in women, with 970, 615 and 729 new diagnoses, respectively, in 2012. The incidence rates were increasing for female lung cancer, male colorectal cancer, and melanoma. By contrast, the rates have been declining for cervix and stomach cancer. For lung cancer and prostate cancer in men and colorectal cancer in women the rates increased, reaching a peak in different periods, and then decreased. The incidence rates of breast cancer rose, reaching a plateau in the mid 2010s. Favorable mortality trends were predicted for all cancers except skin melanoma and lung cancer in women. The prevalence of cancer was increasing with the only exception of cervical cancer in women and lung cancer in men in the most recent estimation period.

Conclusion. The scenario found for cancer incidence and prevalence was largely influenced by screening activities, so that increasing or stable incidence rates may reflect active preventive efforts. Aging, screening, and more complex and costly treatments pose a problem of sustainability and selection of interventions to the regional oncology system. Evaluation of effectiveness of intervention and cost-benefit analyses will be important to ensure cancer control in the future.

Key words: cancer, incidence, mortality, prevalence, model-based estimates, cancer registry, Umbria.

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Introduction

Umbria is a small region located in central Italy with a population of about 900,000 (51.8% females)[1]. The region lies in the interior of the Italian peninsula and has no coastlines. The Apennines chain dominates the Umbria territory, which is mostly hilly (63%) and mountainous (31%).

Population aging is a prevailing phenomenon in Umbria: people ≥65 years old represent over 23% of the inhabitants. Thus Umbria has one of the oldest populations in the world. Aging is due to both low fertility and longevity. Immigration is responsible for the positive growth ratio of the population. As of 2009, foreign-born immigrants accounted for over 10% of the population[1].

With a GDP per capita of 23,531 euro in 2009, Umbria ranks slightly lower than the Italian average and the other central regions[2]. The service industry and secondary sector are the main activities. Some large firms are present in the region (e.g. cement and steel works) but small to medium-sized firms are prevailing (e.g. textile works, food processing, pottery). Agriculture has some importance as well: olive oil, wine, and black truffle are renowned regional products.

The regional health system is almost entirely public. It is articulated into 4 local health units and 2 main hospital trusts, despite the small size of the regional population. The overall number of hospitals is also large (over 20 public hospitals and 5 private hospitals). The oncology system is spread widely over the regional territory with many specialized departments and day-care centers. The hub-and-spoke model was introduced to ensure quality and equity of care independent of type of health structure and place of access to the oncology system. The oncology departments of the 2 main regional hospitals are the hubs of the network. A regional cancer registry, covering the whole Umbria population, was established in 1994 and is now integrated in the oncology network[3,4].

Organized screening programs against cancer of the breast and uterine cervix (started in 1999), and colorectal cancer (started in 2006) are active throughout the regional territory. Opportunistic screening is also widespread for prostate cancer[5] and to a lesser extent skin melanoma[6].

Cancer was responsible for about one third (2,742) of all deaths occurring in Umbria in 2009. The standardized (European standard population) mortality rates were 203 and 118 per 100,000 inhabitants per year among males and females, respectively[7]. If we consider the more recent cancer registry data available (2009), prostate cancer showed the highest incidence rate (age-standardized rate 91 per 100,000) among males, followed by colorectal cancer (67 per 100,000) and lung cancer (55 per 100,000). Breast cancer ranked first (101 per 100,000) and large bowel second (41 per 100,000) among females.

This paper will describe the incidence, prevalence and mortality trends during the period 1970-2015 for the major cancer sites (lung, stomach, colon-rectum, breast, prostate, cervix uteri and skin melanoma) in the Umbria region. The estimates were obtained by applying the MIAMOD[8-10] statistical back-calculation method to survival and mortality data, and will be presented for the selected cancer sites for the Umbria region.

Material and methods

The MIAMOD method, as already described elsewhere in detail[8,9], 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 proportions (per 100,000) for the period 1970-2015. All estimates were carried out up to age 99 years.

Briefly, the MIAMOD method 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)[11]. 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[12]. The survival estimates for the central Italian macro area were assigned to Umbria for all cancer sites except stomach and colon-rectum in males, for which the region-specific survival was applied because of the substantial difference compared with overall survival in the central Italian area. 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)[13], 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 large 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.*[14,15], 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 not have been reliable.

For prostate cancer, a specific procedure was used to capture recent rapid variations of time trends, as suggested by the most recent cancer registry data[16]. Mortality estimation up to 2010 was preliminarily performed by means of the PIAMOD method[17] so as to complete the missing mortality time series in the years 2004 and 2005[11], 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.

Estimated incidence rates were further validated by comparison with observed standardized incidence rates (European standard) obtained from the regional cancer registry of the Umbria Region.

Results

Estimates for the main descriptive epidemiological indicators in 2012 in Umbria by gender are shown in Tables 1A and 1B. In terms of standardized incidence and mortality rates and of prevalence proportion, breast cancer by far ranked first among the female cancers considered. Among males lung cancer was estimated yet to be responsible for the heaviest burden in terms of mortality in 2012. When we look at the prevalence proportions, prostate cancer ranked first. Finally, the highest incidence rate in males was estimated for large bowel cancer. The incidence of large bowel cancer was projected to overtake the prostate cancer incidence in 2011. Colorectal cancer had high values of all indicators in both sexes and thus was responsible for a major health burden in Umbria.

Model-based estimates of time trends for the study indicators over the period 1970-2015 are shown in Figures 1-6. The standardized incidence trends for males and females are reported in Figure 1 and Figure 2, respectively. The standardized mortality trends are illustrated in Figures 3 and 4. The time trends of crude prevalence proportions in men and women are shown in Figure 5 and Figure 6, respectively.

The model-based estimates were close to the cancer–registry-observed incidence data for most sites. For a few cancer sites some discrepancy was found and these results are shown in Figure 7.

The results will be described below, grouped by cancer site.

Stomach

The present analysis confirmed the secular trend for gastric cancer. Incidence and mortality rates were decreasing over the whole period 1970-2015 in both sexes. As for 2015, the age-standardized mortality rates were predicted to be as low as 12.4 per 100,000 among males and 8.6 among females.

Colon and rectum

The incidence of colorectal cancer was estimated to be stable among females since the early 1990s. A very different trend was expected among males, with standardized incidence increasing over the entire period 1970-2015. Colorectal cancer was already more frequent in males at the beginning of the study and a widening gap by gender was expected for large bowel cancer. Mortality rates showed a decreasing trend in both sexes in the more recent study period. However, among males mortality started to decrease a few years later than in females.

Lung

The lung cancer incidence and mortality curves showed closely similar trends. In men, incidence and mortality were decreasing from the early 1990s. In women the lung cancer incidence and mortality were increasing over the study period and in 2015 the expected mortality (13.8 per 100,000) was nearly as high as the breast cancer mortality (15.6) and, according to this prediction, lung cancer would become the second most frequent cause of cancer death in women.

Skin melanoma

The increasing incidence trend of skin melanoma was projected to continue until 2015 in both sexes. The mortality rates were much lower than the incidence rates. Mortality among males was estimated to peak in 1998 and slightly decrease thereafter. Among women mortality increased slightly over the study period.

Breast

Female breast cancer initially showed an increasing incidence trend then reached a plateau in the mid 2010s. The age-standardized rates were expected to rise from 41.2 cases per 100,000 women per year in 1970 to 110.2 in 2015. Mortality rates reached a peak of 25 deaths per 100,000 in 1989 and decreased thereafter. In 2015 breast cancer was yet expected to rank first among the cancer mortality rates but it will be much closer to the lung and colorectal cancer mortality rates.

Cervix uteri

Cancer of the uterine cervix was estimated to have decreasing incidence and mortality trends over the entire study period.

Prostate

The prostate cancer incidence showed 3 distinct trends. Before the 1990s, the incidence was slowly increasing. A steeply increasing incidence was estimated in the period 1989-2003. A decreasing trend was estimated for the period 2003-2015. The mortality rates increased slowly from 17 to 19 per 100,000/year between 1970 and 1998 and then were projected to gradually decrease to 12 per 100,000 in 2015. The incidence/mortality ratio was 1.7 at the beginning of the study period and increased to 5.4 by 2015.

Prevalence

The prevalence of cancer was increasing, with the exception of cervical cancer in women and lung cancer in men in the most recent estimation period. However, prevalence proportions for cancers with no screening and a poor prognosis like gastric cancer and even more lung cancer were estimated to increase much less than the colorectal, prostate and breast cancer prevalence.

Discussion

Model-based estimates of cancer trends are useful for health policy makers. The predicted figures represent what will happen in the future if the relations already present in the observed data will continue in the subsequent years for which data are estimated. The reliability of the predicted scenario depends, of course, on model fit and assumptions. In some instances health policy makers could consider effective interventions to avoid that a predicted health burden will come true. In other cases health programmers may consider the predicted data unlikely, due to changes in health determinants occurring after the period considered in the analyses. In general, flexible parametric models, like those used for this analysis, provide us with nicely smoothed curves that are more suitable to illustrate the gradual change in incidence rates due to risk factors (e.g., the results for gastric cancer and lung cancer were excellent) than the irregular and swifter incidence variations linked to the spread of cancer screening (Figure 7). Indeed, screening for breast, cervix, prostate and colorectal cancer may affect the relationships between epidemiological indicators, which is the base of our models.

For example, the expected, steeply increasing curve for breast cancer, reflecting the introduction of organized breast cancer screening and leading to a standardized incidence peak at about 120 per 100,000 in 2001[18], was smoothed out in the modeled incidence curve. As another example, the spread of PSA-based opportunistic screening and the associated overdiagnosis[19] led to an increase in survival not related to specific mortality. The prostate cancer incidence largely reflects screening intensity, and cancer registry data show a more irregular incidence trend than the one that was captured by the presented model[20].

Risk factors are the main determinants of the trends for lung and gastric cancer. Tobacco smoking is by far the greatest risk factor for lung cancer. The present analysis confirms the opposite trends for lung cancer in male and female incidence and mortality rates reported by other studies[21]. The smoking prevalence as reported by ISTAT[22] in Umbria was slightly lower than the Italian average (e.g. current smokers in 2011 were 21.6% *vs* 22.3%). The 2010 Passi annual report[23] estimated that male and female current smokers accounted for 34% and 30%, respectively. If we compare subsequent annual reports from the Passi survey, the prevalence of smokers seems clearly increasing among females and stable after 2007 in males. This observation is of course alarming and confirms that lung cancer mortality is almost completely determined by exposure to tobacco smoking, at least until the early years 2000s, despite improvement in cancer treatment.

Gastric cancer is an important health problem in Umbria, where a high risk area is present[24]. The secular declining trend, despite the absence of organized interventions, is slowly lowering the health burden due to stomach cancer. Modification of diet and of *Helicobacter pylori* circulation may explain the decreasing gastric cancer trend observed in many areas including Umbria[25,26].

Organized screening programs were introduced in the whole region for breast cancer and cancer of the uterine cervix (both started in 1999) as well as cancer of the large bowel (started in 2006). The introduction of organized screening in 1999 led to a peak in the breast cancer incidence curve (corresponding to the prevalence round) that was already increasing, and then to some variability of incidence in recent years. Mortality was decreasing since 1990 mainly due to improved treatment[27].

As the result of screening activities, the incidence of cervical cancer in Umbria is low. Opportunistic screening based on the offer of a free Pap test was introduced in the 1970s. Organized screening to increase participation and improve quality was introduced in 1999. About 85% of women in the age class 25-64 reported that they had received a Pap test within 3 years in 2009 and 61% of the same women declared that they had undergone testing as part of the organized screening program[28]. The high participation in cervical cancer screening was confirmed by a recent report of the National Observatory on Screening[29]. Adherence to cervical screening by immigrant women will be the key to confirm the favorable mortality and incidence trends predicted, as immigrant women represent an important and increasing percentage of the 25- to 64-year-old population and their adherence to cervical cancer screening is significantly lower than that of women born in Italy[28].

The start of colorectal cancer screening based on immunological fecal occult blood testing has had no effect on the data used in this paper because it started in 2006, i.e. too late to affect the mortality and survival data reported herein. However, such screening will hopefully have an impact on the incidence, survival and mortality of colorectal cancer[30]. Removal of premalignant colorectal lesions should lead to an incidence decrease that will require many years to become apparent and will depend on screening adherence by the Umbrian population. This could modify the predicted increasing incidence among males and the slightly decreasing incidence trend among females. The screening-associated mortality reduction requires some years to become apparent after the start of the intervention (4 at least), so that also mortality will hopefully decrease more than predicted[31].

Epidemiological indicators for prostate cancer are heavily influenced by screening. Prostate cancer screening based on serum PSA testing has not been introduced in Italy as an organized program but its use as a spontaneous or opportunistic diagnostic activity is widespread[5]. The incidence data from the regional cancer registry show irregular variations that may reflect the conflicting scientific evidence published in the literature. Thus great uncertainty affects the modeling and predictions of incidence trends for this cancer. The prostate cancer mortality has been reported to be decreasing in many Western countries[32] due to treatment improvement and screening. The present modeling exercise predicted a lasting decreasing trend in Umbria starting in 2004 and 2001 for prostate cancer incidence and mortality, respectively.

Melanoma of the skin was becoming more frequent in both sexes and this trend was predicted to continue until 2015. The incidence of skin melanoma depends both on early diagnostic activities (i.e. self-detection and opportunistic screening) and on risk factors. Population exposure to risk factors like voluptuary sun exposure and particularly intermittent sunburns has increased in the past years and may be partly responsible for the observed incidence trends[33]. In Umbria there is indirect evidence of a limited spread of early diagnosis (low incidence and survival rates) and also increasing mortality trends both in males and females[6]. The estimated incidence rates were high when compared with cancer registry data (Figure 7), particularly among females, and this result was likely due to the use of the macro area relative survival in the models, influenced by screening activities in neighboring regions. Estimates of the mortality trends showed some improvement and even a slight decrease among males.

Prevalence is an epidemiological indicator that is useful for health policy making and health care organization. The number of cases is relevant to estimate the needs of the health system. It is, however, a rough measure since marked variations in health care needs occur at different times from diagnosis and depending on cancer site. Breast cancer, prostate cancer and colorectal cancer rank highest among the prevalent cancers in Umbria. It is of note that screening activities are widespread for all these cancers.

In conclusion, mortality rates were decreasing for most cancer sites considered. These trends result from different factors including risk factor exposure (e.g., lung cancer in males and gastric cancer), screening (e.g., cancer of the uterine cervix), a combination of treatment improvement and, perhaps, early detection activities/screening (e.g., breast cancer and prostate cancer), early detection awareness and treatment improvement (e.g., colorectal cancer). Lung cancer and melanoma of the skin among females were projected to increase in the coming years if the present risk factor trends will persist. Cancer screening is increasingly used to improve cancer control. The Umbria health system was able to introduce organized programs to prevent breast, cervical and large bowel cancer mortality. Opportunistic screening to prevent prostate cancer and, to a lesser extent, melanoma is also widespread in the region in the absence of structured interventions. Screening activities and improved treatments are responsible for the high prevalence estimates of many cancer types including breast cancer and prostate cancer. We cannot interpret as a merely negative fact the increasing disease frequency for some cancer sites since these trends are the result of efforts to improve health outcomes. However, population aging, cancer screening, and more complex and costly treatments pose a problem of sustainability and selection of interventions to the regional oncology system. Evaluation of the effectiveness of interventions and cost-benefit analyses will be important to ensure cancer control in the future.

Table 1A - Estimated incidence, mortality and prevalence by cancer site for the year 2012 in Umbria. 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	615	141.7	74.0	132	30.3	13.4	5,335	1,230.0
Stomach	169	43.8	24.3	104	26.9	14.1	1,107	288.0
Colon-rectum	554	144.1	78.4	199	51.7	26.3	3,708	964.7
Lung	327	84.9	45.0	286	74.4	38.4	812	211.1
Melanoma	97	25.2	18.4	12	3.0	1.9	862	224.3

Table 1B - Estimated incidence, mortality and prevalence by cancer site for the year 2012 in Umbria. 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	729	177.0	109.9	155	37.7	17.0	9,507	2,308.5
Stomach	145	35.3	14.9	95	23.0	9.1	761	184.9
Colon-rectum	416	101.0	41.2	144	34.9	12.8	3,147	764.2
Lung	150	36.5	18.5	112	27.3	13.0	388	94.4
Melanoma	171	41.5	27.9	13	3.3	1.5	1,671	405.9
Cervix	27	6.5	5.0	11	2.7	1.7	282*	68.6*

*Limited-duration prevalence at 15 years.

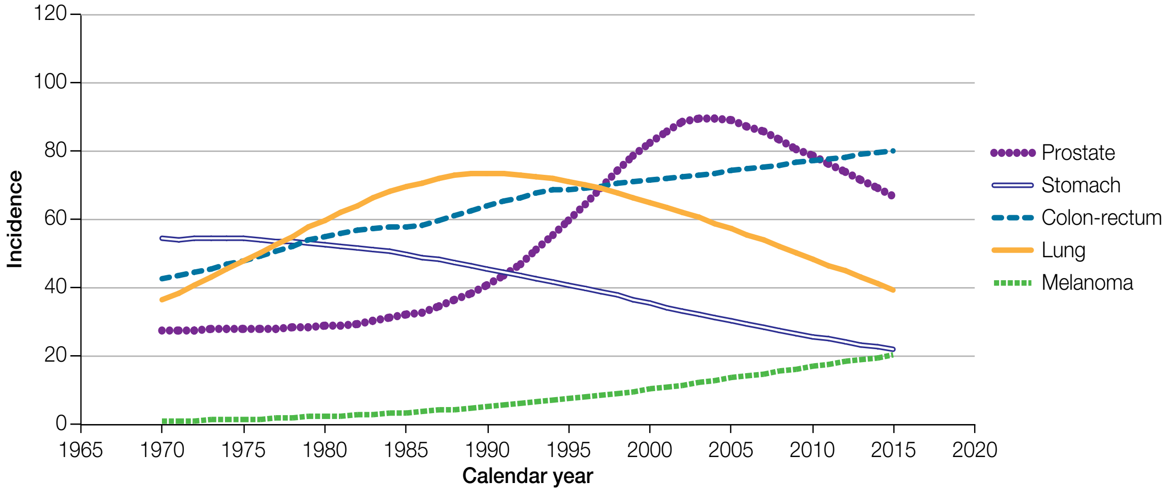


Figure 1 - Incidence estimates by cancer site in Umbria in the period 1970-2015. Age-standardized rates (European population) per 100,000 person-years. Age 0-99 years, men.

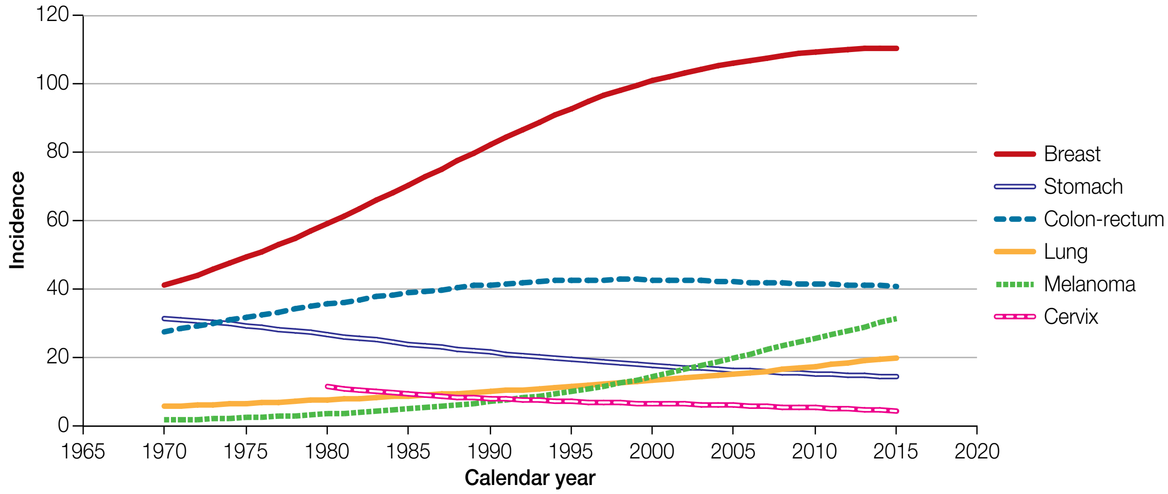


Figure 2 - Incidence estimates by cancer site in Umbria in the period 1970-2015. Age-standardized rates (European population) per 100,000 person-years. Age 0-99 years, women.

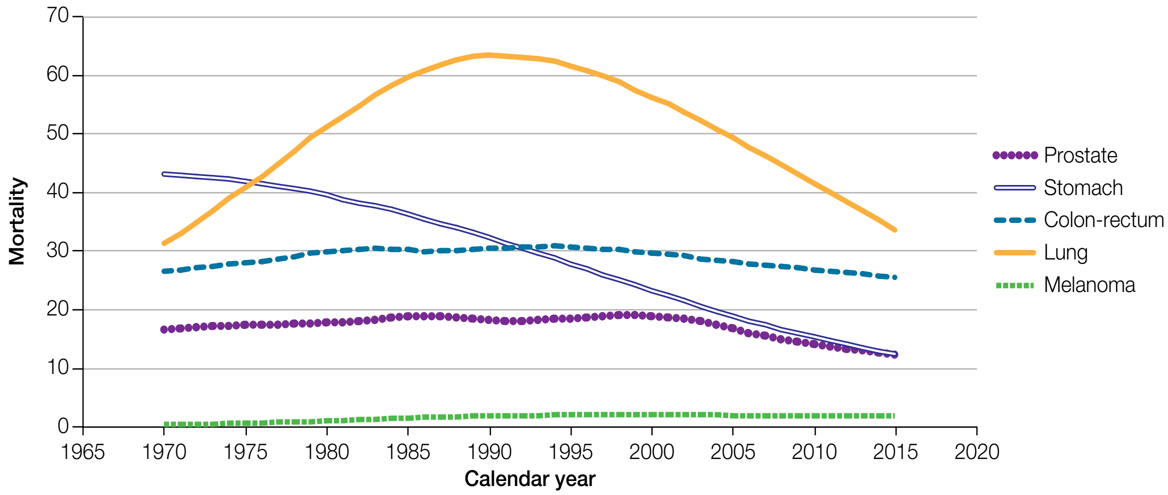


Figure 3 - Mortality estimates by cancer site in Umbria in the period 1970-2015. Age-standardized rates (European population) per 100,000 person-years. Age 0-99 years, men.

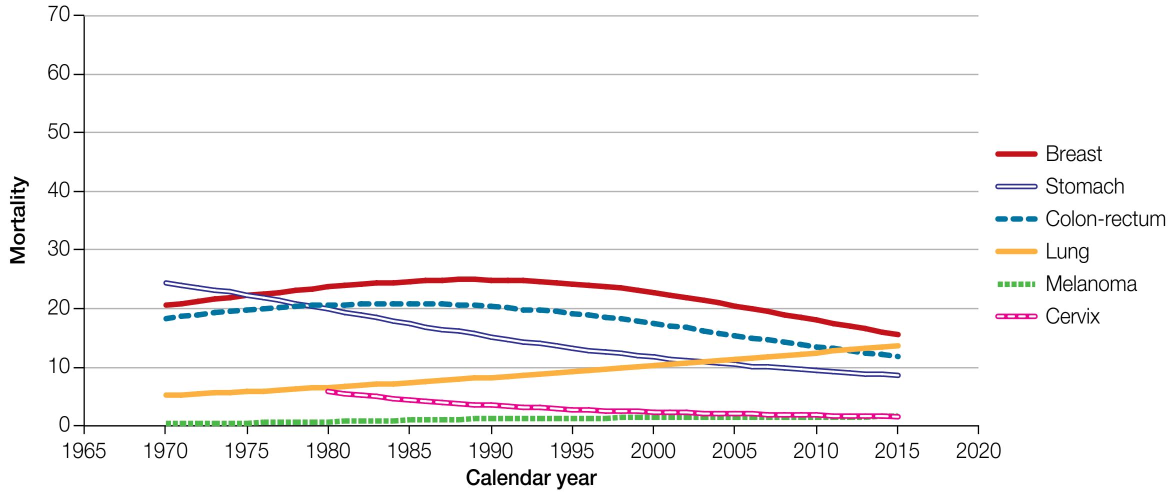


Figure 4 - Mortality estimates by cancer site in Umbria in the period 1970-2015. Age-standardized rates (European population) per 100,000 person-years. Age 0-99 years, women.

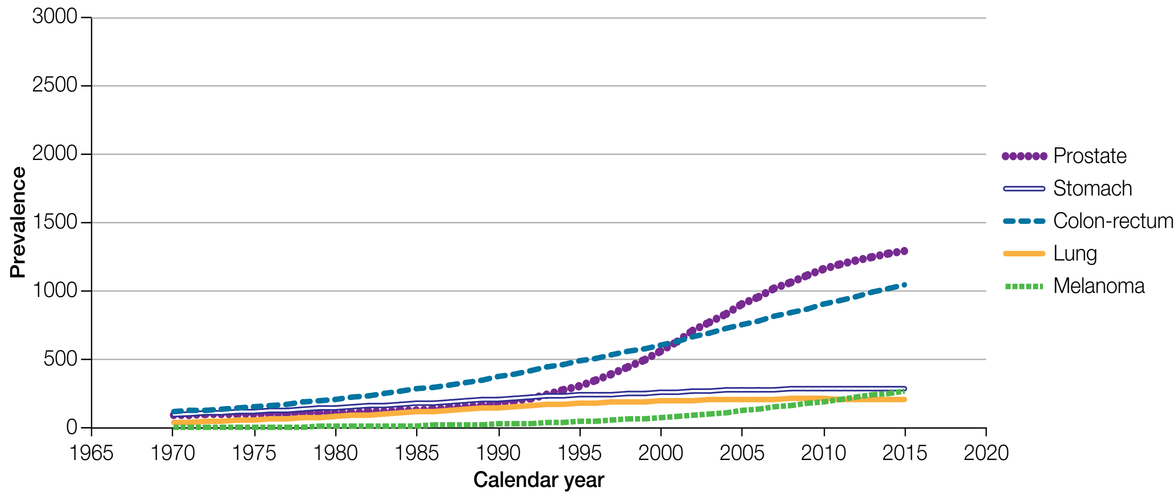
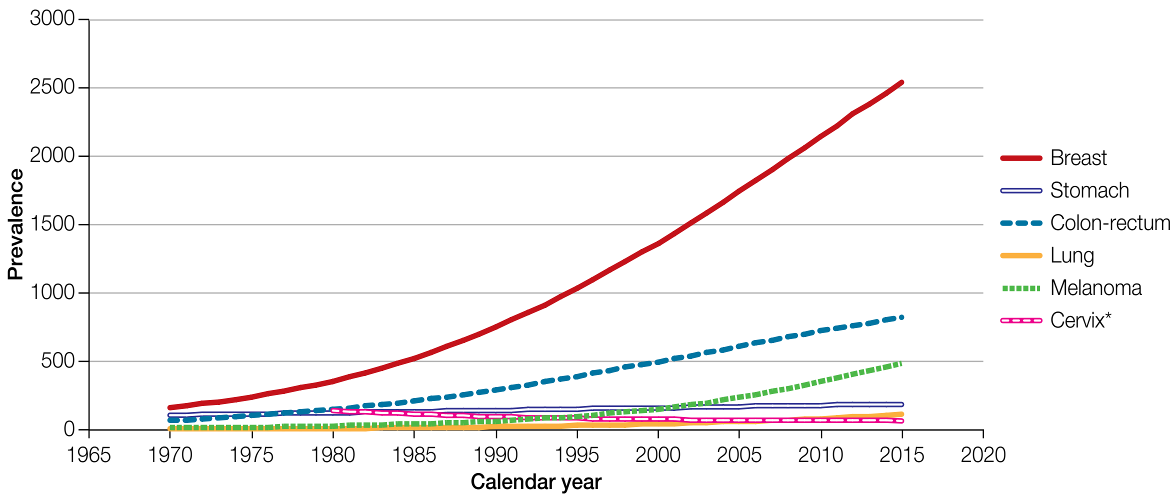


Figure 5 - Prevalence estimates by cancer site in Umbria in the period 1970-2015. Crude proportion per 100,000 persons. Age 0-99 years, men.



**limited-duration prevalence at 15 years*

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

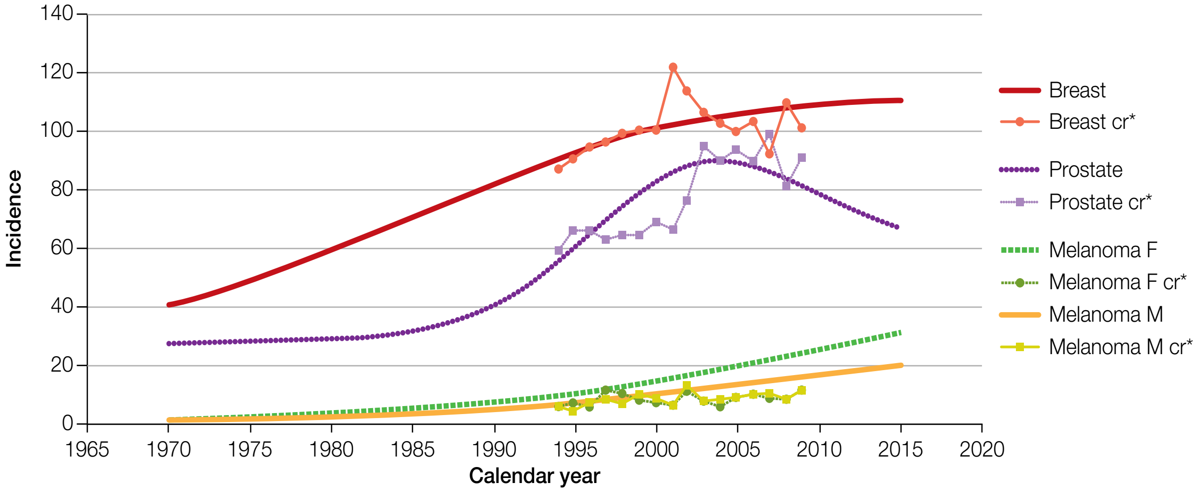


Figure 7 - Incidence, model-based estimates and observed cancer registry data for selected cancer sites. Age-standardized rate (European population) per 100,000 person-years. Age 0-99 years. M, males; F, females.
*cr = Umbria cancer registry data.

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