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Estimates of cancer burden in Tuscany

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ABSTRACT

Aims and background. The Tuscan cancer registry has been operating since 1985, providing cancer incidence and survival data in Tuscany; it covers about 33% of the regional population. The purpose of this paper is to provide incidence, prevalence and mortality estimates for the major cancers in the whole Tuscany region for the period 1970-2015.

Methods. The estimated figures were obtained by applying the MIAMOD method. Starting from mortality and survival data, incidence and prevalence were derived using a statistical back-calculation approach. Survival was modeled on the basis of published data from the Italian cancer registries.

Results. According to the estimates, the most frequent cancer sites were colon-rectum in both genders, prostate in men and breast in women, with 4,188, 3,082 and 3,092 new diagnoses, respectively, in 2012. The incidence rates were steadily increasing for lung cancer in women and melanoma in both sexes, while they were decreasing for uterine cervix cancer in women, lung cancer in men and stomach cancer in both sexes. For colorectal cancer a small reduction in incidence was estimated for both sexes in recent years. The incidence rates for prostate cancer, after a steep increase and subsequent stabilization, were estimated to increase slightly in the last years. The breast cancer incidence was estimated to stabilize in the last 10 years. The mortality trends were decreasing for all considered cancers except female lung cancer. Prevalence increased for most of the studied cancers except stomach cancer in both sexes, lung cancer in men and cervix cancer in women. The highest prevalence was estimated for breast cancer, with over 42,000 cases in 2012.

Conclusion. This paper provides an updated description of the cancer burden in Tuscany until 2015. These trends will have a significant impact on the regional health services and it is therefore important to enhance both primary prevention, for reducing the cancer incidence, and oncological surveillance, for evaluating the care and assistance of cancer patients.

Key words: cancer, incidence, Tuscany, prevalence, mortality, registries, estimates.

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Introduction

The Tuscany region is located in the center of Italy. In 2010 it had a population of over 3,700,000, accounting for about 6% of the national population[1]. The regional health care system is served by 12 local health districts and 4 university hospitals. More than 50,000 professionals including medical doctors, nurses and technical supporters are operating in 40 hospitals and other regional health structures. The treatment of cancer is provided by the health care services participating in the Tuscany Cancer Institute (ITT), a network-based institute conducting also cancer research, which started its activity in 2005. The ITT is constituted by the Florence Cancer Research and Prevention Institute (ISPO) and 16 oncology departments within the local health units, with a total of 216 day-hospital beds and 109 inpatient beds[2].

The Tuscan Cancer Registry (TCR) has been active from 1985 and covers the provinces of Florence and Prato. The main objective of TCR is to provide cancer incidence, survival and mortality data in partnership with the Regional Mortality Registry. The current coverage of TCR is about 33%[3], but there are plans to extend coverage to the entire region; a feasibility study has been conducted and approved.

In 2006 the main cause of death in Tuscany was cardiovascular disease, with about 38% and 44% of deaths in men and women, respectively. Cancer was responsible for about 6,800 (35%) and 5,100 (25%) deaths in men and women, respectively[4]. The Tuscany age-standardized mortality rate for all cancer types was slightly lower than the rate for Italy as a whole (138 per 100,000 *versus* 143 per 100,000)[5].

The purpose of this paper is to provide the basic epidemiological indicators, i.e. incidence, prevalence and mortality, in the Tuscany region for the major cancers (lung, breast, prostate, colon-rectum, stomach, cervix uteri and skin melanoma) 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 period 1970-2002 were obtained from the Italian National Institute of Statistics (ISTAT)[6]. Only specific mortality data for the subsequent years, i.e. 2003, 2006 and 2007 (data for 2004-2005 were not yet published by ISTAT), were used to validate the expected mortality projections[6]. Relative survival data for the considered cancers for the period of diagnosis 1985-2002 were obtained from the EUROCARE-4 study[7]. These data refer to the populations covered by 21 cancer registries in Italy jointly representing about 25% of the national population. Table 1 reports the figures of cancer registration in Tuscany, with the respective area and size of the population covered, the corresponding coverage of the regional population, the percentage of people older than 65 years, and the data collection period.

The MIAMOD method[8-10] 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 patient survival. The method relies on the mathematical relationships between mortality, prevalence, incidence and survival. The model's 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)[11]. 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. The geographical area and the age of patients 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 parameter or a set of area-specific parameters representing the effect of the period of diagnosis depended on the tumors and the sex[10]. The survival estimates for the Central Italian macro area were assigned to Tuscany for all cancer sites with the exception of melanoma in women, for which the region-specific survival was considered. The survival time trend after 2002 was assumed to have the same tendency as that estimated over the observation period 1985-2002 for all cancers except prostate cancer, where survival was assumed to be constant from 2005 onwards.

All incidence, mortality and prevalence estimates were carried out for the period 1970-2015 and 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 specific methodology[12,13] was used to correct for misclassification with uterus not otherwise specified (NOS) in mortality data provided by the official statistics. This methodology could be applied from 1980 onwards because previously the ICD-8 classification, which did not distinguish uterus NOS, had been adopted in the ISTAT statistics. The corrected mortality data 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 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 was reported. Indeed, complete prevalence is highly sensitive to the past trends. Incidence estimates before 1980 are scarcely reliable due to the subsequent spread of non-organized early diagnosis and to the fact that neither mortality nor cancer registry data exist to support reliable modeling assumptions. Simple backward linear extrapolation of the decreasing trend estimated during the 1980s and 1990s may inflate the past incidence level and consequently (due to the high survival) the estimated prevalence of women with a diagnosis of cervical cancer.

For prostate cancer, because of the rapid changes in the recent time trends, more up-to-date mortality data were used in order to capture recent variations that could not be modeled with data up to 2002. Since mortality data for 2004-2005 were missing, estimates with projections up to 2010 were preliminarily performed by means of the PIAMOD method[14]. The modeled mortality was then used as input for the MIAMOD method.

For melanoma different procedures for men and women were adopted to obtain the best incidence estimates in agreement with the observed data by cancer registry. For men the projections of age-specific incidence and mortality rates for melanoma were obtained by linearly projecting the age-specific annual percent change of incidence and mortality rates estimated in

the period 2001-2002. The total rates were obtained by age-specific rates. For women, estimates were obtained using different input data for the MIAMOD method; in particular, mortality data for the period 1987-2008 deriving from the regional mortality registry were used. 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 Tuscany for the year 2012 are presented in Tables 2A and 2B, respectively, for men and women. In the male population prostate cancer was the most frequent cancer with about 3,080 estimated new diagnoses. The incidence of the other cancers was lower, ranging between 2,292 (colon-rectum) and 504 (melanoma) estimated new cases. In women 3,092 new cases of breast cancer were estimated to be diagnosed in 2012. For the other cancers, the numbers of estimated new cases were considerably lower and ranged between 1,896 (colon-rectum) and 98 (cervix uteri). Due to the different survival the ratio between prevalent and incident cases was higher for cancer sites with a better prognosis, like breast cancer for women (14) and prostate cancer for men (8), differently from lung and stomach cancer where the prevalence/incidence ratios were lower for both sexes (3 and 5, respectively, in men and 3 and 6 in women).

The highest crude mortality rates were estimated for lung cancer in men (88 per 100,000) and colorectal cancer in women (38 per 100,000), while the lowest rates were estimated for melanoma in both sexes and cancer of the uterine cervix in women. For colorectal, lung and stomach cancer, the crude mortality rates were higher in men than in women, while for melanoma they were similar, 3.7 and 3.5 per 100,000 for men and women, respectively. With regard to the standardized mortality rates, the male/female ratio was 3.6 for lung cancer, 1.8 for colorectal cancer, and 1.9 for stomach cancer.

The time trends of the age-standardized incidence and mortality rates and crude prevalence 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

The incidence and mortality trends for stomach cancer were estimated to decrease markedly during the whole period. In men, incidence and mortality decreased from 77 and 66, respectively, per 100,000 in 1970 to 18 and 11 in 2015. The trends in women were similar and the rates were lower than in men.

Colon and rectum

For colorectal cancer the male standardized incidence rates were estimated to rise until the end of the 1990s (from 43 per 100,000 in 1970 to 72 per 100,000 in 1999), stabilizing at around 74 per 100,000 and then decreasing slightly in the final years of the considered period (72.7 per 100,000 in 2015). Trends in women were similar, preceding the male trends by some years. The incidence rates in women were always lower than in men, decreasing from 44 to 42 per 100,000/year during the period 2005-2015. The mortality trends reflected the incidence trends but preceding them by a decade and with a more pronounced rate of decrease. The projected mortality rates in 2015 are about half the values observed during the mid 1980s for both genders.

Lung

The lung cancer incidence rates in men reached their peak during the late 1980s (with a maximum rate equal to 93 per 100,000 in 1986-87) and decreased thereafter down to 47 per 100,000 in 2015. In women they increased from 7 per 100,000 in 1970 to 18 per 100,000 in 2015. Due to the very poor prognosis of this cancer, the mortality trends closely mimic the estimated incidence trends. In women, lung cancer was estimated to have reached the breast cancer mortality rate by 2015 (around 13 per 100,000).

Skin melanoma

The melanoma incidence rates were estimated to increase uniformly in both genders. A more than 10-fold increase in men, from 2 to 25 per 100,000/year during the period 1970-2015, and a 3-fold rise in women, from 7 to 22 per 100,000/year between 1987 and 2015, were estimated. The mortality rates were low for both genders as a result of the high survival of melanoma patients. In men they reached a peak in the late 1990s and tended to decrease slightly thereafter. In women the trend was stable at around 1.6 per 100,000/year during the entire period of estimation.

Breast

The breast cancer incidence in women was estimated to increase rapidly from 44 per 100,000 in 1970 to about 104 in the early 2000s. In the subsequent years the growth slowed down and the incidence rate was estimated to stabilize at around 107 per 100,000. The mortality rates, after a slight initial increase from 23 per 100,000 in 1970 to 27 per 100,000 in 1985, were declining steadily to a foreseen level of 13 per 100,000 in 2015.

Cervix uteri

During the study period the incidence and mortality rates of cervical cancer markedly declined, reaching the lowest figures among the cancers considered: 3.9 and 1.3 per 100,000, respectively, in 2015.

Prostate

The incidence of prostate cancer was estimated to increase from 28 to 103 per 100,000/year during the whole

study period. Mortality was estimated to remain stable from 1970 to 2003 at around 18 per 100,000 and to decrease to 14 per 100,000 by 2015.

Prevalence

Prevalence increased for all the considered cancers except stomach cancer in both sexes, lung cancer in men, and cervix cancer in women. In men, the prevalence of both stomach and lung cancer was estimated to decline in the final years of the estimation period, from 2008 and 2010 onwards, respectively. In women, the prevalence of stomach cancer was estimated to decrease from 1983 onwards while for cervix cancer the 15-year limited-duration prevalence was estimated to decrease during the entire study period.

Discussion

The incidence estimates for the major cancers in the Tuscany region computed by means of the MIAMOD method on the basis of the relative survival and observed mortality in the period 1970-2002, projected up to 2015, seem in good agreement with the observed incidence provided by the feasibility study for the regional cancer registry in Tuscany for the year 2004 for those cancer sites where the observed data were available (breast, colon-rectum, lung)[15]. The observed trends in the area of Florence and Prato for the period 1985-2006 are in good agreement with the trends presented in this paper[15].

The trends of the incidence rates showed a constant increase for lung cancer in women and melanoma in both sexes. The incidence trend for prostate cancer, after an increase between 1990-2000, reached a plateau in 2010 and then showed a new slight increase in the final years of projection. At the opposite end, the incidence trends were decreasing for lung cancer in men, cervix cancer in women, and stomach cancer in both sexes. The trend for colon-rectum cancer showed a constant increase up to the late 1990s for men and the late 1980s for women, while in the following years a stabilization and a small reduction was estimated in both sexes.

These incidence trends could be partially related to changes in individual lifestyles. The different lung cancer trends in men and women can be interpreted in terms of the corresponding well-known trends in tobacco smoking, which increased among women and decreased among men during the last 10 years[16]. In Tuscany the proportion of smoking women was higher than the national rate in 2009 (20% *vs* 17%). By contrast, the proportion of Tuscan male smokers was slightly lower than the Italian rate (29% *vs* 30%)[17].

Diet has been indicated as a risk factor for stomach, colorectal, breast and prostate cancer. The consumption of vegetables and fruits is known to be protective against some cancers, whereas obesity for breast cancer, alcohol for breast and colorectal cancer, and salted or smoked preserved foods for stomach cancer are factors that raise the incidence[18]. Except for alcohol consumption the nutritional habits in Tuscany are slightly better than the average behavior in the other Italian regions. The percentage of obese people (BMI ≥30) is significantly lower than the national level (8% *vs* 10%), with a slightly higher value among men than women[17]. The proportion of people that consume 2-4 servings of vegetables or fruit per day is about 70% against a national value of 64%. By contrast, the proportion of Tuscan people that consume at least one alcoholic drink a day is slightly higher than the national value (73% *vs* 69%)[17].

Organized screening for cervix, breast and colorectal cancer has been implemented in each of the 12 local health units, with an invitation percentage of 94% for cervical cancer screening, 90% for breast cancer screening and 78% for colorectal cancer screening, and compliance rates of 55%, 71% and 53%, respectively, in 2009[19]. Screening can have a complex impact on incidence trends, whereas it is expected that mortality decreases after the implementation of efficacious screening programs. The effect on incidence depends on the kind of lesion detected (precancerous *versus* invasive or *in situ*) and the possible occurrence of overdiagnosis. In Tuscany organized screening for breast cancer by mammography every 2 years has been offered to all resident women aged 50-69 years since 2000. For colorectal screening all resident men and women aged 50-69 have been invited for fecal occult blood testing every 2 years since 2005. For cervical cancer Pap tests have been offered to all resident women aged 25-64 years every 3 years since 2004. In some areas of the region the screening program was introduced a few years earlier. Some recently published papers have shown the effect of screening on cancer incidence and mortality. Costantini *et al.*[20] showed the effect of colorectal cancer screening by fecal occult blood test in reducing the colorectal cancer mortality by 2.7% per year in 2 districts of the Tuscany region which began the screening programs in the 1990s, without any evidence of an effect on its incidence. The slight decrease in the regional incidence trend reported in this paper for both sexes in the last years can hardly be attributable to the effect of screening because the implementation of the programs in the entire region was too recent. Puliti *et al.*[21], performing a case-control study, showed that the introduction of breast cancer screening programs in some regions of Italy, including Tuscany, was associated with a 45% reduction of the probability of dying of breast cancer among screened women. It has been shown also that overdiagnosis for breast cancer was limited (1-13%)[22]. This conclusion is in agreement with the trends of estimated incidence and mortality for breast cancer; indeed, the incidence was increasing before the introduction of the screening program and then stabilized, while the mortality showed a marked decline after the imple-

mentation of screening. Zappa *et al.*[23] in a case-control study in Florence demonstrated the effect of the Pap test in reducing the incidence and mortality of cervical cancer. The decreasing trend reported in this paper reflects the impact of screening.

The incidence of skin melanoma has been increasing in Italy over the last years, in Tuscany as well as the other regions[24,25]. Crocetti *et al.*[26] showed an increase both in invasive melanoma (annual percent change: +5.1) and melanoma *in situ* (annual percent change: +11.1) in the area of the TCR. The main reasons suggested in the scientific literature to explain this phenomenon are increased ultraviolet exposure and early diagnosis thanks to heightened public awareness of the warning signs of melanoma and screening by clinicians. This justifies the rising trend modeled by MIAMOD, even if the projected estimates up to 2015 are to be confirmed.

The huge increase in the prostate cancer incidence was largely due to the spread of PSA testing and to opportunistic screening. Since this increase was not accompanied by a corresponding increase in mortality, overdiagnosis has been suggested as the main reason for the increasing trend. In Tuscany the incidence started to decline in 2003[27]. Long-term projections indicating a new increase after 2012 are to be considered with caution.

Prevalence is the best epidemiological indicator to evaluate the cancer burden and is therefore important for the organization of health services. In 2012 the highest prevalence in Tuscany was estimated for prostate cancer (over 24,000 prevalent cases) and female breast cancer (about 43,000 prevalent cases). Taking together all cancer sites analyzed in this paper, individuals with a diagnosis of cancer (new or old) amounted to about 52,000 men and 68,000 women. The estimates appear to be consistent with the Italian cancer figures, reported in 2010 by the AIRTUM working group, for the cancer sites analyzed[28].

Healthier habits, screening programs and therapeutic improvements are modifying the burden of cancer in the Tuscany region. The mortality rates are declining for all cancers except female lung cancer. The number of prevalent cases for all cancer sites is progressively increasing due to the increased cancer incidence and/or longer survival. The only way to reduce the incident cases, and consequently the prevalent cases, remains primary prevention.

Table 1 - Tuscany population, proportion of the elderly population in 2009 and cancer registry with its coverage and beginning of activity

		Population	Population ≥65 years of age %	Coverage %	First year of incidence
Region	Tuscany	3,730,130	23.2		
Registry	Firenze-Prato	1,240,036	22.9	33.2	1985

Table 2A - Estimated incidence, mortality and prevalence by cancer site for the year 2012 in Tuscany. 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	3,082	171.9	99.0	549	30.6	14.5	24,108	1,344.2
Stomach	637	39.4	20.1	426	26.3	12.9	3,408	210.4
Colon-rectum	2,292	141.5	73.8	775	47.9	23.8	15,541	959.6
Lung	1,636	100.9	53.9	1,431	88.2	46.0	4,151	256.0
Melanoma	504	31.1	23.0	60	3.7	2.3	4,621	285.5

Table 2B – Estimated incidence, mortality and prevalence by cancer site for the year 2012 in Tuscany. 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	3,092	177.9	107.9	569	32.8	14.8	42,729	2,457.9
Stomach	486	28.0	11.0	321	18.4	6.8	2,693	154.9
Colon-rectum	1,896	109.1	42.9	653	37.6	13.5	14,022	806.6
Lung	626	36.0	17.9	475	27.3	12.8	1,761	101.4
Melanoma	528	27.7	17.9	67	3.5	1.6	5,701	299.5
Cervix*	98	5.7	4.2	44	2.6	1.4	1,036*	59.9*

*Limited-duration prevalence at 15 years.

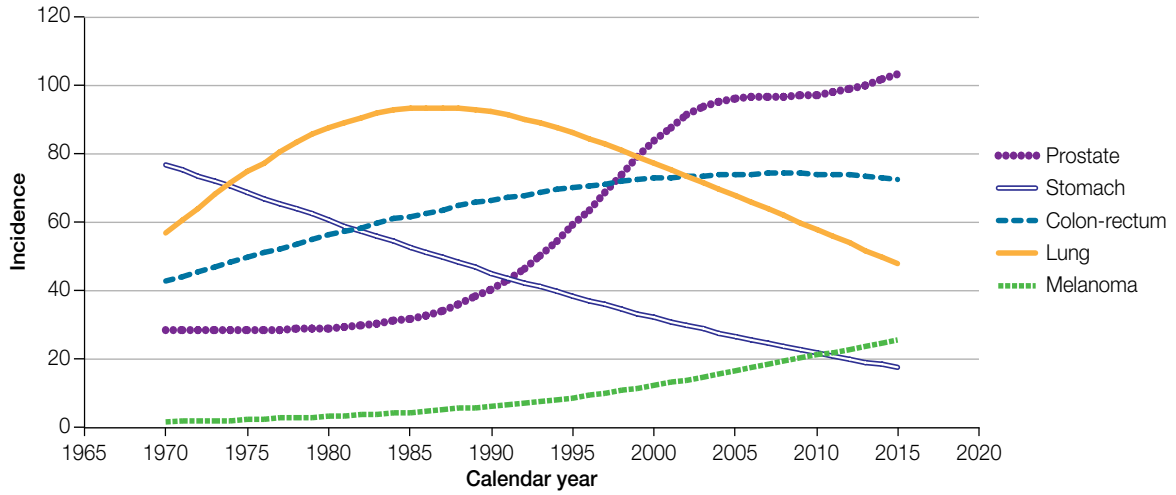


Figure 1 - Incidence estimates by cancer site in Tuscany in the period 1970-2015. Age-standardized rates (European population) per 100,000 person-years. Age 0-99 years, men.

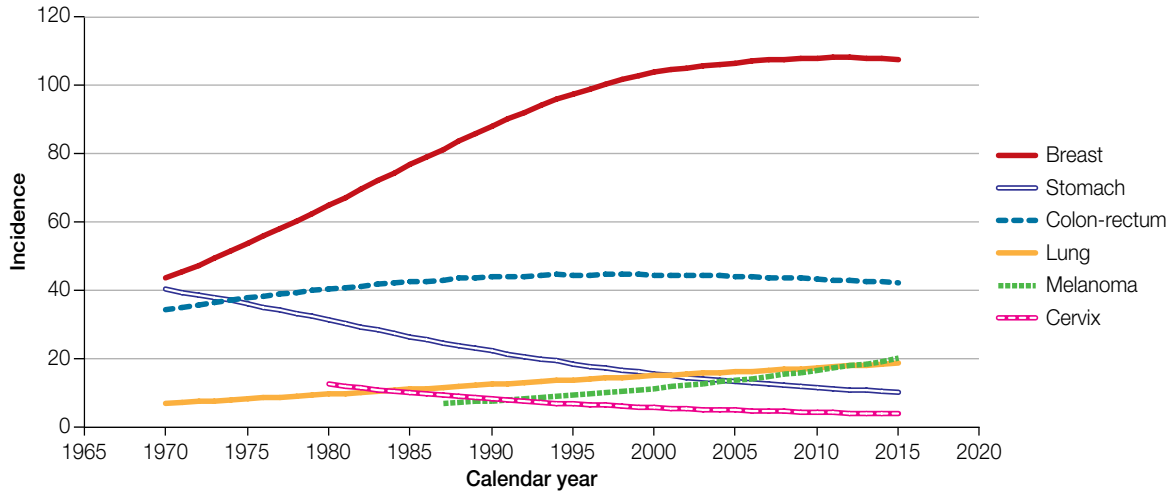


Figure 2 - Incidence estimates by cancer site in Tuscany in the period 1970-2015. Age-standardized rates (European population) per 100,000 person-years. Age 0-99 years, women.

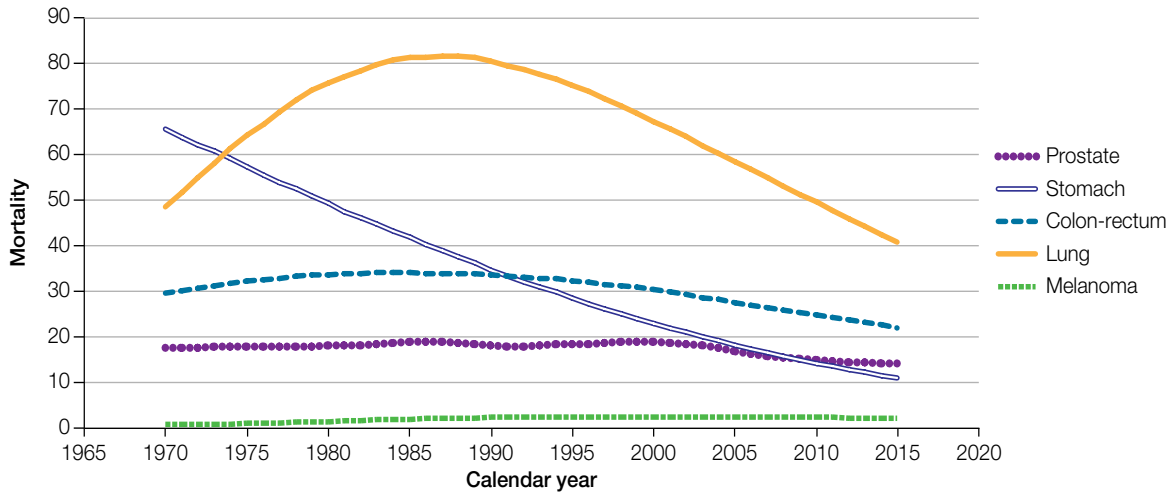


Figure 3 - Mortality estimates by cancer site in Tuscany in the period 1970-2015. Age-standardized rates (European population) per 100,000 person-years. Age 0-99 years, men.

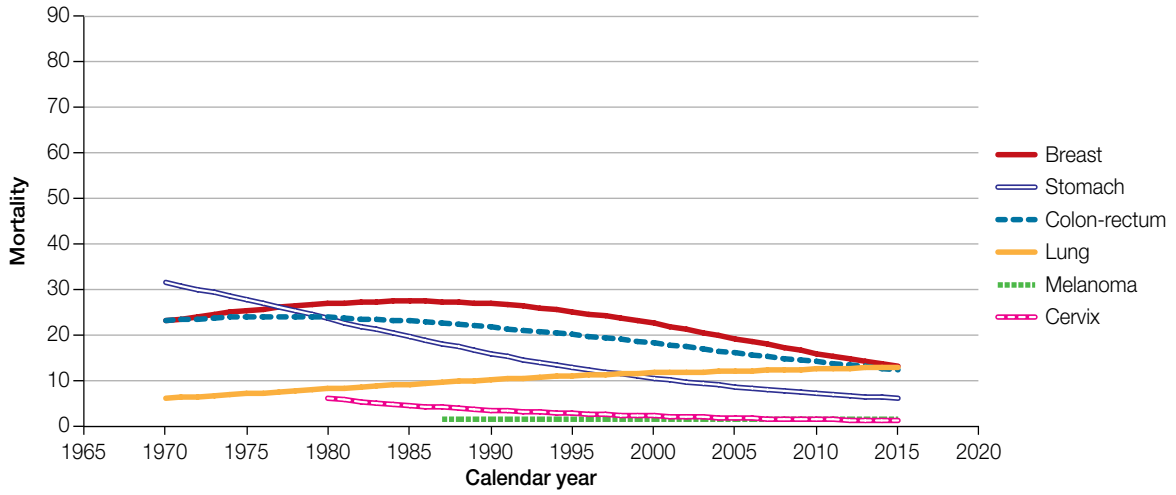


Figure 4 - Mortality estimates by cancer site in Tuscany in the period 1970-2015. Age-standardized rates (European population) per 100,000 person-years. Age 0-99 years, women.

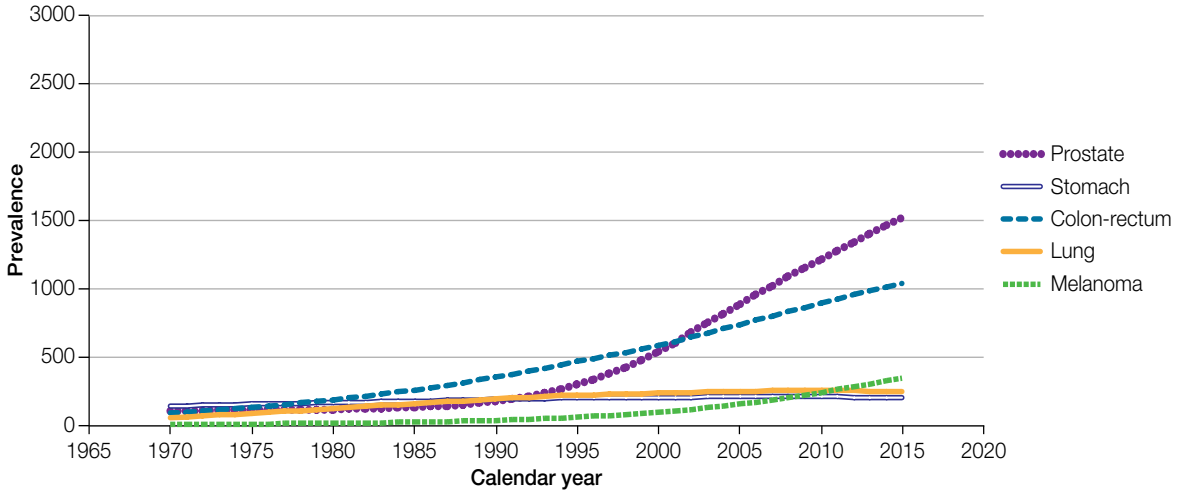
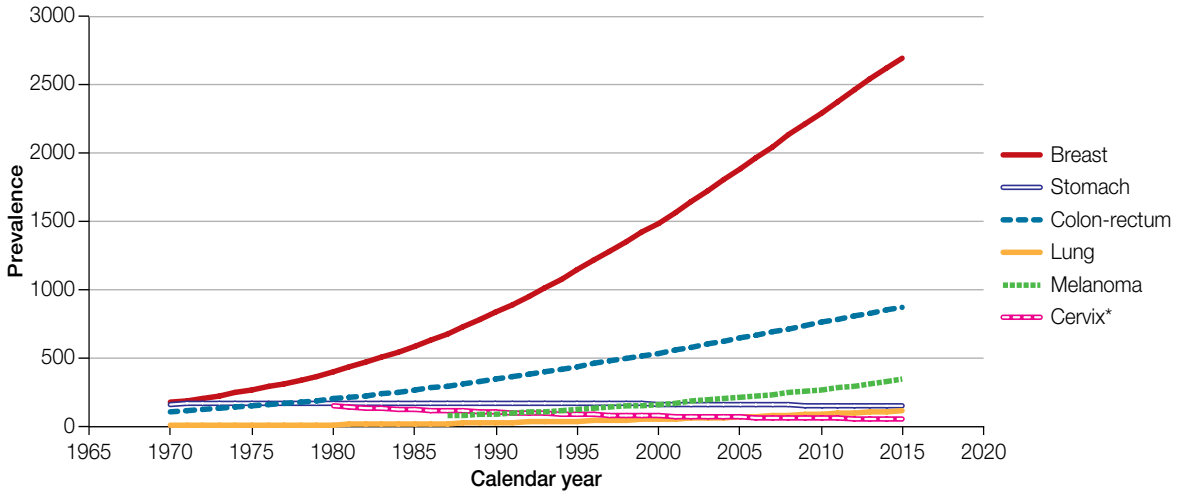


Figure 5 - Prevalence estimates by cancer site in Tuscany in the period 1970-2015. Crude proportion per 100,000 persons. Age 0-99 years, men.



**limited-duration prevalence at 15 years*

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

References

1. ISTAT: Popolazione residente 2010. http://www.demo.istat.it/pop2010/index.html (accessed 8 March 2013).
2. Regione Toscana website. http://www.regione.toscana.it/sst (accessed 8 March 2013).
3. Paci E, Crocetti E, Benvenuti A, Buzzoni C, Caldarella A, Giovannetti L, Giusti F, Intrieri T, Manneschi G, Miccinesi G, Sacchettini C: Cancer incidence in Florence and Prato (1998–2002). In: Cancer incidence in five continents, Vol IX, Curado MP, Edwards B, Shin HR, Storm H, Ferlay J, Heanue M, Boyle P (Eds), IARC Scientific Publications No. 160, IARC, Lyon, 2007.
4. Morti per causa: anno 2006. A cura del Servizio Statistica della Regione Toscana e Registro Mortalità Regionale. Edizioni Regione Toscana, Firenze, 2007.
5. Grande E, Inghelmann R, Francisci S, Verdecchia A, Micheli A, Baili P, Capocaccia R, De Angelis R: Regional estimates of all cancer malignancies in Italy. Tumori, 93: 345-351, 2007.
6. ISTAT: Statistiche sulle cause di morte anno 2008. http://www.istat.it/dati/dataset/20110412_00/ (8 March 2013).
7. Capocaccia R, Gavin A, Hakulinen T, Lutz JM, Sant M (Eds): Survival of cancer patients in Europe, 1995-2002: the EUROCARE-4 study. Eur J Cancer, 45: 901-1094, 2009.
8. Verdecchia A, Capocaccia R, Egidi V, Golini A: A method for the estimation of chronic disease morbidity and trends from mortality data. Stat Med, 8: 201-206, 1989.
9. De Angelis G, De Angelis R, Frova L, Verdecchia A: MIAMOD: a computer package to estimate chronic disease morbidity using mortality and survival data. Comput Methods Programs Biomed, 44: 99-107, 1994.
10. Verdecchia A, De Angelis R, Francisci S, Grande E: Methodology estimation of cancer incidence, survival and prevalence in Italian regions. Tumori, 93: 337-344, 2007.
11. World Health Organization: International classification of diseases, 9th ed, WHO, Geneva, 1997.
12. Capocaccia R, Martina L, Inghelmann R, Crocetti E, De Lisi V, Falcini F, Guzzinati S, Rosso S, Tagliabue G, Tumino R, Vercelli M, Zanetti R, De Angelis R: A method to estimate mortality trends when death certificates are imprecisely coded: an application to cervical cancer in Italy. Int J Cancer, 124: 1200-1205, 2009.
13. De Angelis R, Rossi S, Martina L, Meduri C, Galati F, Capocaccia R: Stime di incidenza e mortalità per cervico-carcinoma in Italia. In: La prevenzione dell'infezione da papilloma virus umano in Italia. Atti del Workshop “La prevenzione dell'infezione da papilloma virus umano in Italia”. Istituto Superiore di Sanità, Rome, 28 September 2009. Rapporti ISTISAN, 10/25: 4-11, 2009.
14. Verdecchia A, De Angelis G, Capocaccia R: Estimation and projections of cancer prevalence from cancer registry data. Stat Med, 21: 3511-3526, 2002.
15. Tuscany Cancer Registry. http://www.ispo.toscana.it (accessed 8 March 2013).
16. ISTAT: I fumatori in Italia. http://www3.istat.it/salastampa/comunicati/non_calendario/20060110_00/ (accessed 8 March 2013).
17. Regional Health Agency (ARS). http://www.ars.toscana.it/marsupio/parsis/ (accessed 8 March 2013).
18. World Cancer Research Fund (WCRF) and the American Institute for Cancer Research (AICR): Food, nutrition, physical activity, and the prevention of cancer: a global perspective. AICR, Washington DC, 2007.
19. I programmi di screening della Regione Toscana, 11th report. http://www.ispo.toscana.it (accessed 8 March 2013).
20. Costantini AS, Martini A, Puliti D, Ciatto S, Castiglione G, Grazzini G, Zappa M: Colorectal cancer mortality in two areas of Tuscany with different screening exposures. J Natl Cancer Inst, 100: 1818-1821, 2008.
21. Puliti D, Miccinesi G, Collina N, De Lisi V, Federico M, Ferretti S, Finarelli AC, Foca F, Mangone L, Naldoni C, Petrella M, Ponti A, Segnan N, Sigona A, Zarcone M, Zorzi M, Zappa M, Paci E; IMPACT Working Group: Effectiveness of service screening: a case-control study to assess breast cancer mortality reduction. Br J Cancer, 99: 423-427, 2008.
22. Puliti D, Zappa M, Miccinesi G, Falini P, Crocetti E, Paci E: An estimate of overdiagnosis 15 years after the start of mammographic screening in Florence. Eur J Cancer, 45: 3166-3171, 2009.
23. Zappa M, Visioli CB, Ciatto S, Iossa A, Paci E, Sasieni P: Lower protection of cytological screening for adenocarcinomas and shorter protection for younger women: the results of a case-control study in Florence. Br J Cancer, 90: 1784-1786, 2004.
24. Curado MP, Edwards B, Shin HR, Storm H, Ferlay J, Heanue M, Boyle P (Eds): Cancer incidence in five continents, Vol IX. IARC Scientific Publications No. 160, IARC, Lyon, 2007.
25. International Agency for Reaearch on Cancer: Cancer Incidence in Five Continents Annual Dataset. http://ci5.iarc.fr/CI5plus/ci5plus.htm (accessed 8 March 2013).
26. Crocetti E, Caldarella A, Chiarugi A, Nardini P, Zappa M: The thickness of melanomas has decreased in central Italy, but only for thin melanomas, while thick melanomas are as thick as in the past. Melanoma Res, 20: 422-426, 2010.
27. Crocetti E, Ciatto S, Buzzoni C, Zappa M: Prostate cancer incidence rates have started to decrease in central Italy. J Med Screen, 17: 50-51, 2010.
28. AIRTUM Working Group: Italian cancer figures, report 2010: Cancer prevalence in Italy. Patients living with cancer, long-term survivors and cured patients. Epidemiol Prev, 34 (5-6 Suppl 2): 1-188, 2010.