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Estimates of cancer burden in Lombardy

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ABSTRACT

Aims and background. Cancer registration in Lombardy covers almost half of the regional population and started in 1976 in the Varese province. The aim of this paper is to provide estimates of the incidence, mortality and prevalence of seven major cancers for the entire Lombardy 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. Published data from the Italian cancer registries were modeled in order to estimate the regional cancer survival.

Results. In Lombardy, about 9,000 new cases of breast cancer, 8,500 of colorectal cancer, 7,200 of prostate cancer and 6,700 of lung cancer were expected to be diagnosed in the year 2012. Incidence rates are still rising for female breast cancer, skin melanoma in both sexes, and lung cancer in women. By contrast, the rates have been declining for cervix and stomach cancer. For lung cancer in men, prostate cancer and colorectal cancer the rates increased, reaching a peak in different periods, and then decreased. Prevalence increased for all cancers considered except cervix cancer. The rise was less pronounced in stomach cancer due to the impressive reduction of its incidence and was striking for breast and prostate cancer, with 116,000 and 58,900 prevalent cases in 2012. Mortality dropped for all considered cancers with the only exception of lung cancer in women.

Conclusion. This up-to-date picture of the cancer risk and burden in Lombardy shows the increasing demand for oncology services as one of the major challenges for the region. However, primary prevention is still the only way to simultaneously reduce incidence, prevalence and mortality rates, thus saving further lives and preserving health resources.

Introduction

Lombardy is the Italian region with the largest population, about 10 million¹. Because the health care organization in Italy is regionalized, the Lombardy health care system can be compared with a national system of a medium-size European country, such as Sweden, Belgium or Austria².

We are dealing with a wealthy region contributing by a proportion higher than 20% to the national GDP³. The population is served by 29 public hospitals, 17 specialist research clinics and 194 private hospitals⁴. Specifically for cancer patients, 1,080 beds are available and 2 specialized cancer hospitals are located in the region: the National Cancer Institute, a public hospital active since the beginning of the last century, and the European Institute of Oncology, a private hospital active since 1994. Both hospitals highly attract patients from outside the region⁴.

Organized screening has been implemented in the entire region for breast and colorectal cancer, and in 6 provinces for cervix cancer as well⁵.

Key words: cancer, cancer registries, incidence, prevalence, mortality, Lombardy, regression analysis.

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Six population-based cancer registries (accredited by AIRTUM, the Italian Association of Cancer Registries) are presently providing incidence data. Five of them are covering the provinces of Brescia, Como, Mantova, Sondrio and Varese, while one is active in the municipality of Milan. At the beginning of 2011, 47% of the regional population was covered by an active accredited registry. Other registries recently started collecting data but have not yet been included in AIRTUM.

Cancer is the second cause of death in Italy but the first in Lombardy, with 16,550 cancer deaths in 2008⁶. The Lombardy age-standardized mortality rate is the highest in the north of Italy (157 per 100,000/year) and, at a national level, the third after Campania and Friuli Venezia Giulia⁷. Consequently, cancer in this region requires major efforts in primary care and resources for social support to patients as well as for indirect costs of cancer, such as the worktime lost by patients and their families.

This paper will provide the basic epidemiological indicators, i.e. incidence, prevalence and mortality, in the Lombardy region for the major cancers (lung, breast, prostate, colon-rectum, stomach, cervix uteri and skin melanoma) in the period 1970-2015. The figures were estimated by applying the MIAMOD statistical back-calculation method to survival and mortality data⁸⁻¹⁰.

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 EURO CARE-4 study¹¹. These data 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 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)¹². The subsequent years, i.e. 2003, 2006 and 2007 (data for 2004-2005 were not yet published by ISTAT), were used to validate the expected mortality projections. Relative survival of cancer patients was estimated from observed cancer registry data by means of parametric cure models of the Weibull type at the level of macro area. 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 term for the period effect on risk or various terms according to geographical areas depended on the tumors and the sex¹⁰. The survival estimates for the northwest of Italy were assigned to Lombardy. 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.

Table 1 shows the cancer registries active in Lombardy, 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. Estimate validation was possible with registries having a relatively long period of observation such as Varese, Milano and Sondrio.

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 specific methodology^{13,14} 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 before that year the ICD-8 classification, which did not distinguish uterus NOS, was 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 this site 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 method¹⁵. The modeled mortality was 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 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. The age-standardized rates were based on the standard European population.

Results

Table 1 shows that Lombardy has a population of about 10 million, 20% of whom over the age of 65 years. Cancer registration began in the late 1970s in the Varese province. At present 6 cancer registries cover about 50% of the regional population.

The number of cases, the crude and age-standardized incidence and mortality rates and the prevalence proportions estimated in Lombardy for the year 2012 are presented in Tables 2A and 2B for men and women, respectively. During this year, prostate cancer was the most frequent cancer in men with about 7,200 estimated new diagnoses. The incidence of the other male cancers was substantially lower, with estimated new cases ranging between 4,830 (lung) and 1,425 (stomach). About 9,000 new cases of breast cancer were expected to be diagnosed in the female population, while for the other cancers the numbers of estimated new cases were considerably lower and ranged between 3,846 (colon-rectum) and 221 (cervix uteri). The breast cancer prevalence figures in women were more than 10 times higher than the incidence figures. The prevalence was only double the incidence for lung cancer in both sexes. The highest crude mortality rates were for lung cancer in men (92 per 100,000) and breast cancer in women (40 per 100,000) and the lowest for melanoma in both sexes and cervix uteri cancer in women. For colorectal, lung and stomach cancer and melanoma, all the indicators were higher in men than women; the highest ratio was reported for lung cancer, slightly more than 3.5, and the lowest ratio for colorectal and gastric cancer (between 1.5 and 2).

The time trends of the 3 indicators over the period 1970-2015 are shown in the Figures. They present the age-standardized incidence in men (Figure 1) and women (Figure 2), the age-standardized mortality in men (Figure 3) and women (Figure 4), and the crude prevalence in men (Figure 5) and women (Figure 6). The results will be described below, grouped by cancer site.

Stomach

The incidence and mortality trends for stomach cancer were estimated to decrease noticeably over the whole period. In men, the incidence and mortality decreased from 77 and 67, respectively, per 100,000 in 1970 to 18 and 12 in 2015. The trends in women were similar and the rates were lower than in men.

Colon and rectum

For colorectal cancer the male incidence rates were estimated to rise until the end of the 1990s (71 per 100,000 in 1999) and to decrease slightly thereafter (65 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 38 per 100,000 during the period

1994-2015. 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 almost half the values observed during the mid 1980s for both genders.

Lung

The lung cancer incidence rates in men reached their peak in the mid 1980s (with a maximum rate equal to 123 per 100,000 in 1984-85) and decreased thereafter. In women they increased up to 20 per 100,000 in 2011. By 2015, the age-standardized lung cancer incidence rates are expected to decrease to 60 per 100,000 for men and to slightly exceed 20 per 100,000 in women. 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 become the second most frequent cause of cancer death after breast cancer after the year 2008.

Skin melanoma

The melanoma incidence rates were estimated to increase for both genders. In men, we estimated a more than 10-fold increase, from 2 to 26 per 100,000/year, during the period 1970-2015, while in women the increase was smaller (from 3 per 100,000 in 1970 to 16 per 100,000 in 2015). Trends were similar between genders until 1994, although lower in men. From 1994 onwards the tendency changed: the male rates increased much more rapidly than the female rates, and for men the incidence was about 30% higher than for women in 2015. The mortality rates were low, as a result of the high survival of melanoma patients. They reached a peak during the 1990s for both genders and tended to decrease slightly thereafter.

Breast

The breast cancer incidence in women was estimated to increase rapidly from 56 per 100,000 in 1970 to about 110 in the early 1990s, and then more slowly up to 123 per 100,000 in 2015. Projections for breast cancer incidence are to be taken with caution, as this indicator reflects more the impact of screening activities than the natural evolution of risk factors. Our projections, based on observations up to 2002, foresee a continuing increase, even if with a less pronounced slope and tending to level off at the year 2015. The mortality rates reached a peak in the mid 1980s (35 per 100,000) and then declined steadily to an estimated level of 18 per 100,000 in 2015.

Cervix uteri

During the study period the age-standardized incidence and mortality rates of cervical cancer decreased markedly, reaching the lowest figures among the cancers considered: 3 and 1 per 100,000, respectively, in the year 2015. Also the prevalence is expected to decrease in the future.

Prostate

The prostate cancer incidence was estimated to increase during the period 1970-2005 from 32 per 100,000 to 106 per 100,000/year. Thereafter the rates seemed to stabilize or slightly decline to reach the rate of 94 per 100,000 in 2015. Mortality for prostate cancer remained stable from 1970 to 2000 and then started to decrease, with an estimated reduction in 2015 of about 30% with respect to the peak level.

Prevalence

Prevalence increased for all cancers considered except cervix cancer. The increase was less pronounced for stomach cancer due to the impressive reduction of its incidence but instead it was striking for breast and prostate cancer. It is interesting to note the opposite behavior for mortality, which declined for all considered cancer sites with the only exception of lung cancer in women.

Discussion

This paper provides an updated description of the burden of the major cancers in the Lombardy region in terms of point estimates in 2012 and time trends through 2015. The comparison between the estimated Lombardy incidence and the data of 3 local cancer registries, available from the AIRTUM database, showed a good match over the time period covered by cancer registration. The results of the validation procedures will be illustrated extensively in a separate report (paper in preparation).

The incidence rates are still rising for female breast cancer, skin melanoma in both genders and lung cancer in women. By contrast, the rates have been declining for cervix and stomach cancer. For lung cancer and prostate cancer in men and colorectal cancer in both genders the rates increased, reaching a peak in different periods, and then decreased.

The major risk factor affecting the observed trends for some of the considered cancers is smoke. Smoke is related to lung, stomach and cervix cancer, with different attributable risks¹⁶. The prevalence of smoking in Italy has been decreasing among men since the 1970s. By contrast, smoking is rising in women¹⁷. The smoking prevalence in Lombardy was fairly stable in the past 10 years, its estimates ranging from 23% according to the ISTAT survey¹⁷ "Health status of the population and use of health services" to 29% as reported by the Passi survey¹⁸. These values are among the highest in northern Italian regions^{17,18}. For stomach, colorectal, breast and prostate cancer, diet is an important risk factor¹⁹. The estimated increasing incidence trends can be associated with modifications in the diet of the Italian population, showing increasing consumption of energy-dense foods and sugary drinks and decreasing consumption of salted or smoked preserved foods¹⁹. We do not have information about food consumption by region; however, the proportion of the Lombardy population that

was overweight or obese (BMI >25%) was 33% in 2010, less than the national average (42%)²⁰.

Screening, whether organized or not, has had a strong impact on the incidence trends of breast, cervical and prostate cancer and, to some extent, also colorectal cancer. In Lombardy, according to the Passi annual report²¹ the access to Pap tests for 25- to 64-year-old women was high (75%) in the late 2000s (at least 1 test in the last 3 years) and the annual percentage of invited women who accepted to be tested, during the same period and for the same age groups, was around 40%²². The same study reported an even higher (86%) access to mammography for 50- to 69-year-old women in the same period (at least 1 test in the last 2 years)²². According to the ISTAT survey, the percentages of women having Pap tests in the 25- to 64-year age group and mammograms in the 50- to 69-year age group increased between 2000 and 2005 from 78% to 81% and from 64% to 82%, respectively.

In 2006 the Ministry of Health included colorectal cancer in the recommendation for screening²³. In the Lombardy region, as in Italy, the access to the screening tests for colorectal cancer was low with respect to the other programs. In a sample of healthy people 50-69 years of age, 62% declared to have had a test (fecal occult blood test or endoscopy) in the last 2 years²². For this tumor, the slight reduction of incident cases cannot be attributed to the start of screening; the changes are more likely to be connected to stabilization of the pattern of risk factors for colorectal cancer and to more widespread knowledge of the risk factors among the population.

As in several Western countries, the incidence of skin melanoma is increasing also in Italy²⁴. Several factors may have contributed to the increase, including raised ultraviolet exposure, increased public awareness of the warning signs of melanoma, and increased screening by clinicians²⁵.

The huge increase in the prostate cancer incidence was largely due to the spread of PSA testing as opportunistic screening. PSA testing started to be widely used in Lombardy at the end of the 1980s²⁶. We cannot say how much of the prostate cancer incidence rise is due to risk factors or to early diagnosis (including overdiagnosis) of prostate lesions. Since the increase was not accompanied by a corresponding increase in mortality, which was quite stable up to 2000 and then decreased slightly, a major contribution of overdiagnosis for this cancer is likely. In Lombardy, like in many Western countries including the US and Nordic countries, the prostate cancer incidence started to decline around 2005²⁷⁻²⁹.

Since the early 1990s the mortality rates for all the considered cancers except lung cancer in women have been declining. Mortality depends on incidence and for lung cancer, with few effective therapeutic options, the mortality rates were very close to the incidence rates. Mortality is also related to survival and to early diagnosis for those cancers that benefit from effective therapy given to patients with localized disease. The reduction of postoperative mortality especially for colorectal,

stomach and prostate cancer³⁰⁻³³ and the more widespread availability of adjuvant hormonal therapy for breast cancer, adjuvant chemotherapy for colon cancer, and neoadjuvant radiotherapy for rectal cancer further contributed to the reduction of mortality³⁴⁻³⁶.

Prevalence measures the burden of cancer in its different phases: treatment, clinical follow-up, palliation and social disabilities. Therefore this indicator is important for the organization of health services. Tables 2A and 2B show that the prevalence is particularly high for prostate cancer and female breast cancer. In 2012 Lombardy was estimated to care for about 116,000 women with a diagnosis (new or old) of breast cancer, about 1 out of 41 women. For the same year we estimated 58,900 prevalent cases of men with prostate cancer: 1 of 82 Lombard men.

Except for lung cancer, where the cessation of smoking is the central goal for reducing mortality, substantial diagnostic and therapeutic resources contributed to the reduction of the mortality rates in Lombardy. Due to the benefit of early diagnosis and screening programs, and partly to the improvement of therapeutic effectiveness, cancer survival will increase in the next years. This phenomenon, added to population aging, will inflate the cancer prevalence. Facing the increasing demand for oncology services is one of the major challenges for the Lombardy region. However, primary prevention is the only way to simultaneously reduce the incidence, prevalence and mortality rates, thereby saving further lives and preserving health resources.

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

		Population	Population ≥65 years of age %	Coverage %	First year of incidence
Region	Lombardy	9,917,714	20	47	1976
Registry	Varese	883,285	21	Province	1976
	Sondrio	183,169	20	Province	1998
	Milan	1,307,495	24	Municipality	1999
	Brescia	1,256,025	19	Province	1999
	Mantova	415,442	21	Province	1999
	Como	594,988	20	Province	2003

*AIRTUM accredited registries; other Lombardy cancer registries include Milano-1 Local Health Agency, Bergamo, Cremona, Lodi, Pavia, Leco, and Monza-Brianza.

Table 2A - Estimated incidence, mortality and prevalence by cancer site for the year 2012 in Lombardy. 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	7,242	150.6	97.1	1,102	22.9	14.1	58,905	1,225.2
Stomach	1,425	32.7	20.4	983	22.5	13.7	7,040	161.3
Colon-rectum	4,691	107.5	67.3	1,670	38.3	23.2	31,532	722.4
Lung	4,830	110.6	69.7	4,002	91.6	56.1	11,570	264.8
Melanoma	1,319	30.2	23.3	159	3.6	2.5	11,822	271.0

Table 2B - Estimated incidence, mortality and prevalence by cancer site for the year 2012 in Lombardy. 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	9,152	198.8	123.1	1,859	40.4	20.0	116,593	2,532.4
Stomach	1,132	24.6	11.2	789	17.1	7.4	5,402	117.4
Colon-rectum	3,846	83.6	38.8	1,389	30.2	13.0	29,080	631.7
Lung	1,911	41.5	20.7	1,467	31.9	15.2	4,269	92.8
Melanoma	939	20.4	15.2	83	1.8	1.0	13,525	294.0
Cervix	221	4.8	3.5	98	2.1	1.3	2,568*	56.0*

*Limited-duration prevalence at 15 years.

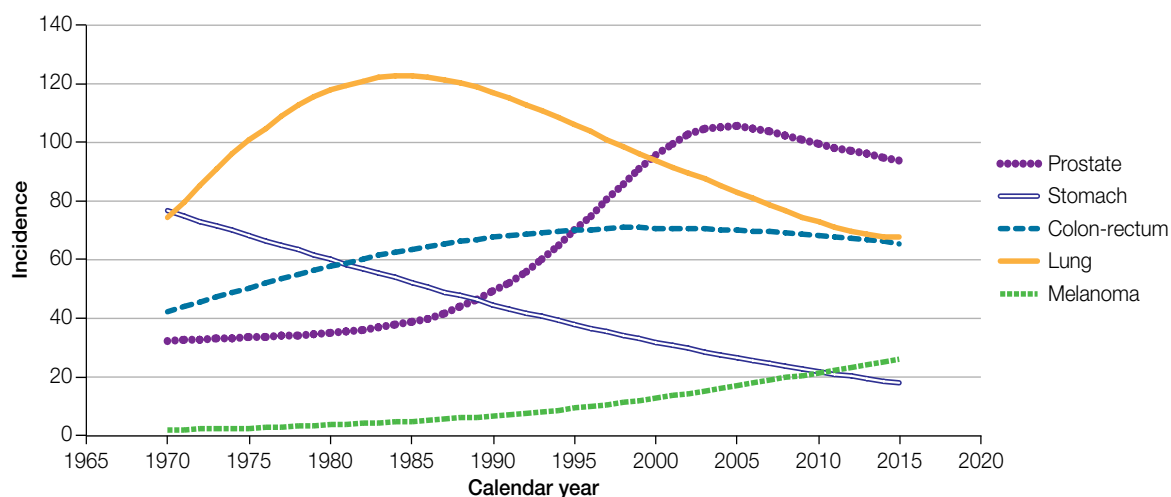


Figure 1 - Incidence estimates by cancer site in Lombardy in the period 1970-2015. Age-standardized rates (European population) per 100,000 person-years. Age 0-99 years, men.

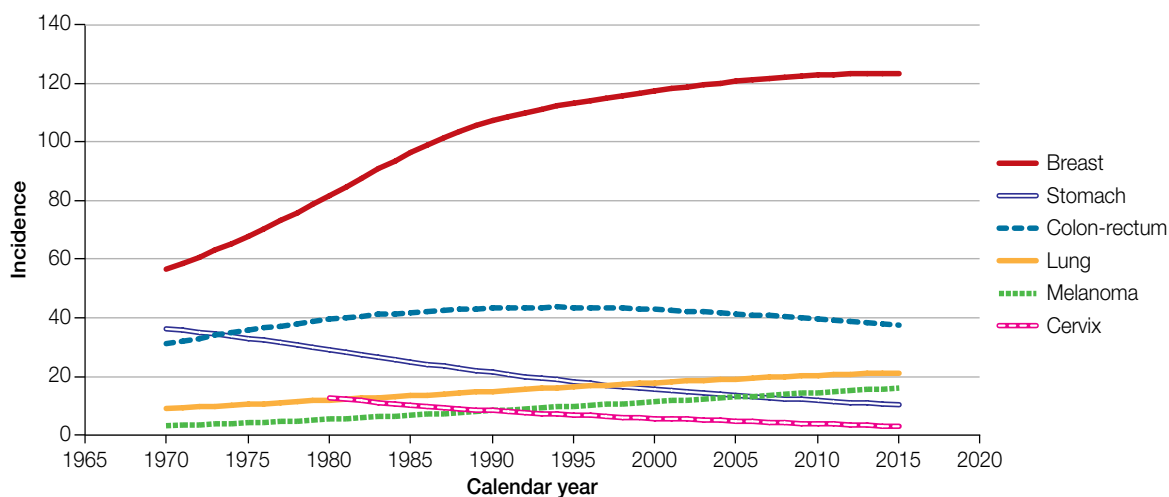


Figure 2 - Incidence estimates by cancer site in Lombardy in the period 1970-2015. Age-standardized rates (European population) per 100,000 person-years. Age 0-99 years, women.

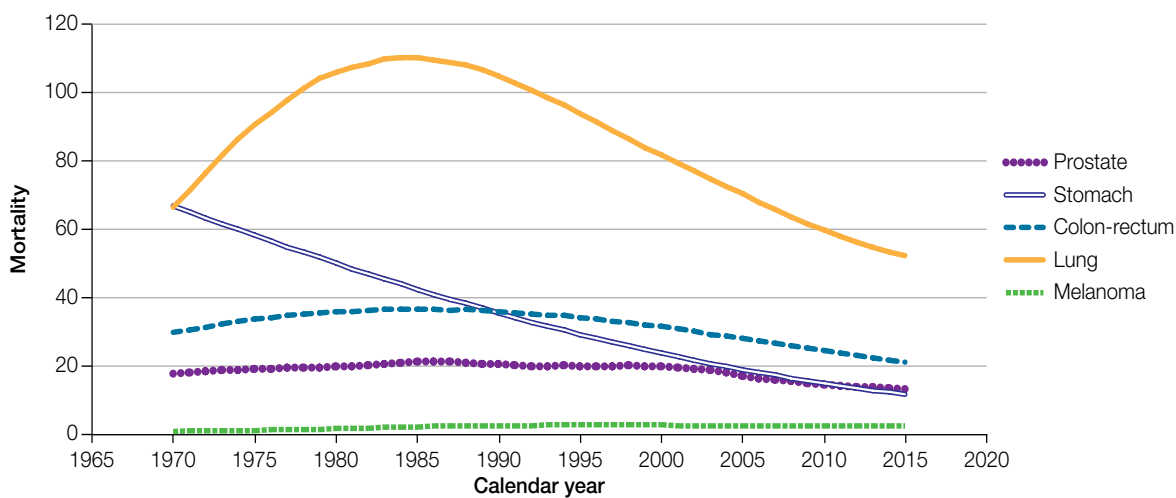


Figure 3 - Mortality estimates by cancer site in Lombardy in the period 1970-2015. Age-standardized rates (European population) per 100,000 person-years. Age 0-99 years, men.

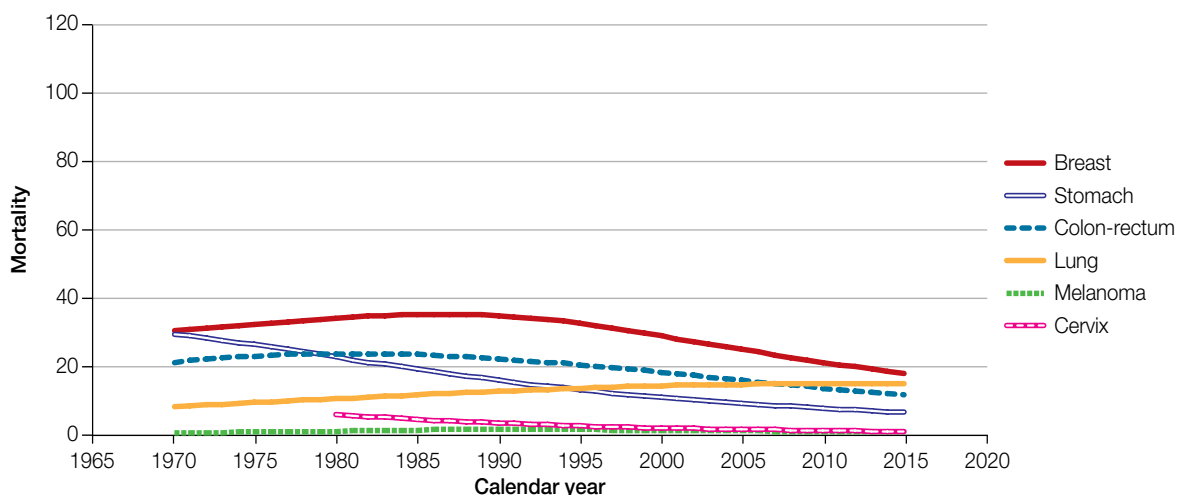


Figure 4 - Mortality estimates by cancer site in Lombardy in the period 1970-2015. Age-standardized rates (European population) per 100,000 person-years. Age 0-99 years, women.

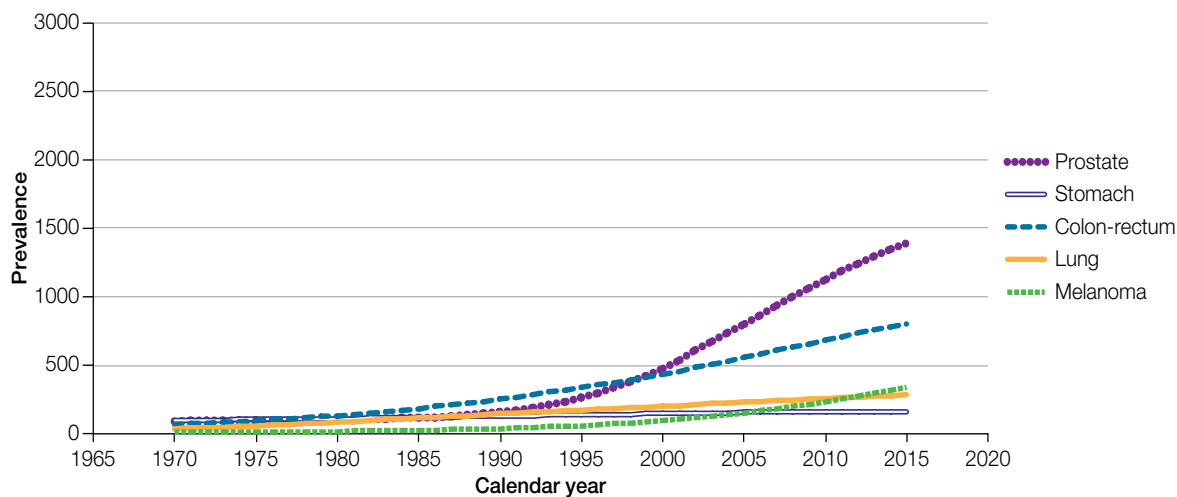
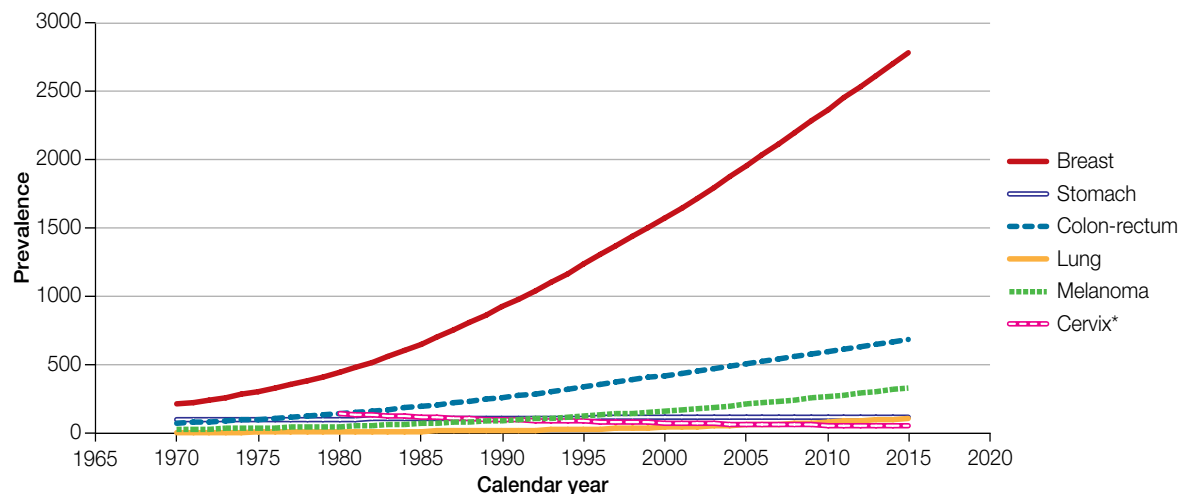


Figure 5 - Prevalence estimates by cancer site in Lombardy in the period 1970-2015. Crude proportion per 100,000 persons. Age 0-99 years, men.



*limited-duration prevalence at 15 years

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

References

1. ISTAT: Popolazione residente 2010. <http://demo.istat.it/pop2010/index.html> (accessed 8 March 2013).
2. EUROSTAT: Statistics pocket book online. Data last updated on 25 March 2011-094023.
3. Annuario Statistico Regionale Lombardia. <http://www.asr-lombardia.it/ASR/conti-economici-territoriali/> (accessed 8 March 2013).
4. Federazione Italiana delle Associazioni di Volontariato in Oncologia (FAVO): Terzo rapporto sulla condizione assistenziale dei malati oncologici promosso dall'osservatorio sulla condizione assistenziale dei malati oncologici, 2011.
5. Osservatorio nazionale screening. <http://www.osservatorionazionalecreening.it/> (accessed 8 March 2013).
6. ISTAT: Statistiche sulle cause di morte anno 2008. http://www.istat.it/dati/dataset/20110412_00/ (accessed 8 March 2013).
7. 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.
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. Capocaccia R, Gavin A, Hakulinen T, Lutz JM, Sant M (Eds): Survival of cancer patients in Europe, 1995-2002: the EURO-CARE-4 study. *Eur J Cancer*, 45: 901-1094, 2009.
12. World Health Organization: International classification of diseases, 9th ed, WHO, Geneva, 1997.
13. 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.
14. 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.
15. Verdecchia A, De Angelis G, Capocaccia R: Estimation and projections of cancer prevalence from cancer registry data. *Stat Med*, 21: 3511-3526, 2002.
16. Gandini S, Botteri E, Iodice S, Boniol M, Lowenfels AB, Maisonneuve P, Boyle P: Tobacco smoking and cancer: a meta-analysis. *Int J Cancer*, 122: 155-164, 2008.
17. European Health For All Database (HFA-DB). World Health Organization, Regional Office for Europe, 2005.
18. Rapporto nazionale Passi 2009: Guadagnare salute. Abitudine al fumo. <http://www.epicentro.iss.it/passi/rapporto2009/Fumo09.asp> (accessed 8 March 2013).
19. 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.
20. Rapporto nazionale Passi 2010. Percentuale di persone in eccesso ponderale. http://www.epicentro.iss.it/passi/rapporto10/eccesso_ponderale.xls (accessed 8 March 2013).
21. Rapporto nazionale Passi 2009. <http://www.epicentro.iss.it/passi/rapporto2009/IndiceRapporto09.asp> (8 March 2013).
22. Osservatorio Nazionale Screening: Gli screening sul campo. <http://www.osservatorionazionalecreening.it/content/gli-screening-sul-campo> (8 March 2013).
23. Ministero della Salute, Direzione Generale della Prevenzione: Screening oncologici. Raccomandazioni per la pianificazione e l'esecuzione degli screening di popolazione per la prevenzione del cancro della mammella, del cancro della cervice uterina e del cancro del colon retto. In attuazione dell'art. 2 bis della Legge 138/2004 e del Piano nazionale della prevenzione 2005-2007, approvato con Intesa Stato Regioni del 23 marzo 2005 Gruppi di lavoro nominati dai Decreti del ministro della salute del 3 novembre 2004 e del 18 ottobre 2005, in applicazione della Legge 138 del 2004 (art 2 bis).
24. International Agency for Research on Cancer: Cancer Incidence in Five Continents Annual Dataset. <http://ci5.iarc.fr/CI5plus/ci5plus.htm> (8 March 2013).
25. Giblin AV, Thomas HM: Incidence, mortality and survival in cutaneous melanoma. *J Plast Reconstr Aesthet Surg*, 60: 32-40, 2007.
26. Quaglia A, Vercelli M, Puppo A, Casella C, Artioli E, Crocetti E, Falcini F, Ramazzotti V, Tagliabue G: Prostate cancer in Italy before and during the 'PSA era': survival trend and prognostic determinants. *Eur J Cancer Prev*, 1282: 145-152, 2003.
27. Kvåle R, Auvinen A, Adami HO, Klint A, Hernes E, Møller B, Pukkala E, Storm HH, Tryggvadottir L, Tretli S, Wahlqvist R, Weiderpass E, Bray F: Interpreting trends in prostate cancer incidence and mortality in the five Nordic countries. *J Natl Cancer Inst*, 99: 1881-1887, 2007.
28. Bray F, Lortet-Tieulent J, Ferlay J, Forman D, Auvinen A: Prostate cancer incidence and mortality trends in 37 European countries: an overview. *Eur J Cancer*, 46: 3040-3052, 2010.
29. Baade PD, Youlten DR, Krnjacki LJ: International epidemiology of prostate cancer: geographical distribution and secular trends. *Mol Nutr Food Res*, 53: 171-184, 2009.
30. Molina JR, Yang P, Cassivi SD, Schild SE, Adjei AA: Non-small cell lung cancer: epidemiology, risk factors, treatment, and survivorship. *Mayo Clin Proc*, 83: 584-594, 2008.
31. Ferjani AM, Griffin D, Stallard N, Wong LS: A newly devised scoring system for prediction of mortality in patients with colorectal cancer: a prospective study. *Lancet Oncol*, 8: 317-322, 2007.
32. Degiuli M, Sasako M, Ponti A; Italian Gastric Cancer Study Group: Morbidity and mortality in the Italian Gastric Cancer Study Group randomized clinical trial of D1 versus D2 resection for gastric cancer. *Br J Surg*, 97: 643-649, 2010.
33. Lowrance WT, Elkin EB, Jacks LM, Yee DS, Jang TL, Laudone VP, Guillonneau BD, Scardino PT, Eastham JA: Comparative effectiveness of surgical treatments for prostate cancer: a population-based analysis of postoperative outcomes. *J Urol*, 183: 1366-1372, 2010.
34. Berry DA, Cronin KA, Plevritis SK, Fryback DG, Clarke L, Zelen M, Mandelblatt JS, Yakovlev AY, Habbema JDF, Feuer EJ: Effect of screening and adjuvant therapy on mortality from breast cancer. *N Engl J Med*, 353: 1784-1792, 2005.
35. Mano MS, Duhoux F: Colon cancer: update on adjuvant therapy. *Clin Colorectal Cancer*, 7: 178-183, 2008.
36. Dobie SA, Warren JL, Matthews B, Schwartz D, Baldwin LA, Billingsley K: Survival benefits and trends in use of adjuvant therapy among elderly stage II and III rectal cancer patients in the general population. *Cancer*, 112: 789-799, 2008.