Estimates of cancer burden in Emilia-Romagna

Fabio Falcini[1], Silvia Mancini[1], Alessandra Ravaioli[1], Rosa Vattiato[1],
Lauro Bucchi[1], Stefano Ferretti[2], Maria Michiara[3], Massimo Federico[4],
Maurizio Ponz de Leon[5], Lucia Mangone[6], Silvia Rossi[7], and Roberto Foschi[8]

[1]Romagna Cancer Registry, IRCCS Romagna Scientific Institute for the Study and Treatment of Tumors (IRST), Meldola (FC); [2]Registro tumori della Provincia di Ferrara, Ferrara; [3]Registro tumori della Provincia di Parma, Parma; [4]Registro tumori della Provincia di Modena, Modena; [5]Registro dei tumori colorettali di Modena, Modena; [6]Registro tumori Reggiano, Reggio Emilia; [7]Centro Nazionale di Epidemiologia, Istituto Superiore di Sanità, Rome; [8]SS di Epidemiologia Valutativa, Fondazione IRCCS Istituto Nazionale Tumori, Milan, Italy

ABSTRACT

Aims and background. This paper aims to provide a comprehensive overview of mid-term epidemiological trends for the major cancer sites in the Emilia-Romagna region of northern Italy (population 4,400,000).

Methods. The MIAMOD method, a back-calculation approach to estimate and project the incidence of chronic diseases from mortality and patient survival, was used for the estimation of incidence and prevalence by calendar year (from 1970 to 2015) and age (from 0 to 99). Survival estimates were taken from cancer registries of northeastern Italy.

Results. The estimated incidence of stomach cancer decreased by approximately 75% for both sexes. Trends in incidence of colorectal cancer differed between males and females. For females, the rate increased moderately until the year 2000 with a slow decrease thereafter, whereas the male colorectal cancer incidence showed a regular increase until 2010 followed by a substantial leveling off. Among males the lung cancer incidence and mortality rates showed a steep increase until the late 1980s and a rapid decrease thereafter. Among females, the trends were increasing over the entire study period. The estimated incidence of female breast cancer rose sharply between 1970 and 2001, but from that year onwards a slightly decreasing trend was observed. Mortality peaked in 1988 and has fallen since. The incidence of prostate cancer showed a 3-fold increase. After 2005, the rate is expected to stabilize. Among females, the estimated prevalence increased for breast cancer (52,700 cases expected in 2015), colorectal cancer, lung cancer and melanoma, while decreasing for stomach cancer and cervical cancer. Among males, the estimates showed an upward trend for prostate cancer (32,100 cases expected in 2015) and colorectal cancer, and a leveling off for lung cancer after 2010.

Conclusion. The estimates were fairly consistent with previous data from several epidemiological sources. The MIAMOD method provided a picture of the impressive increase in the prevalence of breast cancer and prostate cancer over the 45-year period studied.

Introduction

The Emilia-Romagna region is located in the northeast of Italy, in the very center of the country's most productive area. In 2010 the population was about 4,400,000[1], amounting to about 7% of the national population.

The Emilia-Romagna Regional Health Service is part of the National Italian Health Service and is subdivided into 11 local health care districts. As of 31 December 2010, public and accredited private hospital beds in the Region totaled 20,759 (15,941 public, 4,818 accredited private). The total number of beds for cancer patients was 463[2]. Two oncology hospitals are located in the region: the Cancer Institute of Romagna (IRST-IRCCS), which is based in Meldola, Forlì, and the cancer Institute of Reggio Emilia (IRCCS).

In the Region, there are 3 ongoing population-based screening programs for the early detection of breast cancer (women aged 45-74), cervical cancer (women aged 25-64) and colorectal cancer (men and women aged 50-69). Breast cancer screening and cervical cancer screening were started in 1996, and colorectal cancer screening in 2005[3].

Five population-based cancer registries are currently operating in the provinces of Parma, Reggio-Emilia, Modena and Ferrara and in the subregion of Romagna (provinces of Ravenna, Forlì, Cesena, Rimini and health care district of Imola). Cancer is the second cause of death in Emilia-Romagna, with 13,600 deaths in 2007. In that year, the Emilia-Romagna age-standardized (based on the European standard population) cancer mortality rate is 218 per 100,000 person-years in men and 129 per 100,000 person-years in women[4].

Material and methods

Mortality data for all cancers, general mortality and population data by age, calendar year and geographical region for the period 1970-2003 and 2006-2007 were obtained from the Italian National Institute of Statistics (ISTAT)[5]. Relative survival data for the considered cancers for the period of diagnosis 1985-2002 were obtained from the EUROCARE-4 study[6]. The data refer to the populations covered by 21 cancer registries in Italy jointly covering about 25% of the national population.

Table 1 reports the cancer registries active in Emilia-Romagna, with the respective area and size of population covered, the corresponding coverage of the regional population, the percentage of people older than 65, and the data collection period.

The MIAMOD method[7-9] was used for the estimation of incidence and prevalence by calendar year (from 1970 to 2015) and age (from 0 to 99). 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)[10]. 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. The 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 survival estimates for the northeast macro area were assigned to Emilia-Romagna. The way of considering year of diagnosis (continuous or categorical) and the choice of having a unique term for period and risk or various terms for each macro area depended on the tumors and the sex[9]. 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.

For cervical cancer, prostate cancer and melanoma, additional procedures were followed to account for specific problems related to these sites. For cervical cancer a methodology was applied[11,12] to derive correct mortality data adjusted for the large and well-known misclassification with uterus not otherwise specified (NOS) in the official statistics. 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. Incidence and prevalence were then estimated by the MIAMOD method using as input the corrected mortality data. 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 Italy. Furthermore, for cervical cancer only limited-duration prevalence at 15 years is reported. Indeed, complete prevalence is highly sensitive to the past trends. For cervical cancer, incidence estimates before 1980 are scarcely reliable because of 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 which could not be modeled with data up to 2002. Since mortality data for 2004-2005 were missing, mortality estimates with projections up to 2010 were preliminarily performed by means of the PIAMOD method[13]. 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 from age-specific rates. The age-standardized rates were based on the standard European population.

Results

The number of cases as well as the crude and age-standardized incidence, mortality and prevalence rates estimated for the Emilia-Romagna region in 2012 are shown in Tables 2A and 2B. The highest incidence and prevalence rates were estimated for prostate cancer among males and breast cancer among females. The number of prevalent female breast cancer cases slightly exceeded 49,500. Lung

cancer and breast cancer were the most common causes of cancer death among males and females, respectively.

Figures 1 to 6 show the time trends of the incidence, mortality and prevalence rates between 1970 and 2015 for both sexes.

Incidence and mortality

The estimated age-standardized stomach cancer incidence decreased by approximately 75% in both sexes (from 79.0 to 19.5 per 100,000/year in males and from 45.6 to 10.3 per 100,000/year in females). The decrease in the estimated mortality rate was even greater: approximately 83% for males as well as females. The male:female ratio was 2.0 both for incidence and mortality.

The estimated incidence trends for colorectal cancer differed between males and females. For females, the rate increased moderately until 2000 with a slow decrease thereafter. Males showed a steady rise in incidence until 2010 followed by a substantial leveling off. The male:female ratio increased progressively up to the current level of 2.0. Mortality rates began to decrease during the 1980s for both sexes, although the trend was more pronounced for females.

Among males the lung cancer incidence and mortality rates (which are very similar due to the high lethality of the disease) showed a steep increase until the late 1980s and a rapid decrease thereafter. The estimated incidence and mortality rates for the year 2015 are lower than those for the year 1970. Among females, both incidence and mortality were on the rise over the entire study period. Between 1970 and 2015, the estimated increase was about 250% for incidence and about 150% for mortality. The male:female ratios have decreased accordingly, with current values of 2.3 for incidence and 2.8 for mortality.

Over the study period, the estimated incidence of melanoma increased progressively up to more than 10-fold. By 2015, the age-standardized rate is projected to exceed 20 per 100,000 persons in both sexes. The increase in mortality has been far more limited, and the current rates are slightly decreasing.

The estimated incidence of female breast cancer rose sharply between 1970 and 2001 (from 48.5 to 109.7 per 100,000 women), but from this year onwards a slightly decreasing trend was observed and the incidence is expected to reach values around 100 per 100,000 by 2015. The estimated trend in mortality has been quite different, with a moderate increase until the 1980s and a peak of 30.5 per 100,000 in 1988, followed by a clear-cut decrease in the most recent years.

Over the study period, the estimated incidence of cervical cancer showed an about 3-fold decrease (from 14.5 to 4.5 per 100,000). This was paralleled by a mortality decrease from 6.3 to 1.4 per 100,000.

The incidence of prostate cancer showed a 3-fold increase, most of which was concentrated in the mid 1980s. After 2005, the rate is expected to stabilize. The mortality rates have moderately decreased since the late 1980s.

Prevalence

In the female population, the estimated prevalence showed increasing trends for breast cancer, colorectal cancer, lung cancer and melanoma, while the opposite estimate was made for stomach cancer and cervical cancer. The largest increase (from 4,000 cases in 1970 to 52,700 in 2015) was that for breast cancer.

As far as males are concerned, a large increase was estimated for prostate cancer (from 1,900 cases in 1970 to 32,100 in 2015). Colorectal cancer also showed an upward trend. The prevalence of lung cancer is expected to level off after 2010. Contrary to females, the trend in the prevalence of stomach cancer has been moderately increasing (from 149.4 to 212.8 per 100,000).

Discussion

This study provided a comprehensive overview of mid-term epidemiological trends for the major cancer sites in Emilia-Romagna. The data are of value for a wide range of research and public health purposes.

Incidence, mortality and prevalence estimates were fairly consistent with previous data made available by several epidemiological sources in the region[4], although these had only a partial coverage in time and space. The only exceptions worthy of note were an underestimate of the incidence of cervical cancer and an overestimate of the incidence of melanoma among females only. These discrepancies will have to be evaluated thoroughly. The incidence of cervical cancer appeared to be substantially below (about -20%) the average level reported by the pool of regional registries for the 1990s, but tended to approach the observed values during the 2000s. This might be interpreted in the light of the characteristics of back-calculation methods, which are relatively insensitive in capturing sudden changes in incidence, particularly those associated with the introduction of an organized screening program or the rapid spread of early detection practices. This could be the case also for breast cancer.

The results regarding colorectal cancer and lung cancer were consistent with other data. In the most recent years, the estimated incidence of colorectal cancer has leveled off among males while starting to decrease among females. The mortality rates began to decrease during the 1980s for both sexes.

Data for lung cancer were also estimated. Among males, the incidence and mortality rates showed a steep increase until the late 1980s and a rapid decrease thereafter. Thanks to its large time span, the study demonstrated that the incidence and mortality rates in 2015 will be lower than those in 1970. Among females, both incidence and mortality rose over the entire study period, with an estimated increase of about 250% for incidence and 150% for mortality. It is worth noting that the male:female ratio in 2015 is expected to be as low as about 2 both for incidence and mortality. Another inter-

esting aspect is that from 2013 the lung cancer mortality is expected to exceed the breast cancer mortality, becoming the leading cause of cancer death among women.

For breast cancer the data showed a marked increase in incidence until 2001 followed by a slightly decreasing trend, while the prevalence rates showed a growing trend throughout the period of study. The Emilia-Romagna organized mammography screening program was rapidly and completely implemented in the second half of the 1990s. The MIAMOD estimates are based on mortality data up to 2002, which only partially reflect the effect of screening. Despite the limitations of the MIAMOD model in the presence of screening programs, this study was able to document the increase in breast cancer incidence before the program was started and showed that the trend in breast cancer incidence is expected to go down in the next few years. The estimated incidence trend reflects that observed by the regional

cancer registries, although with a lower level because MIAMOD does not take into account screen-detected early diagnosis. The estimated incidence in this case can be read as a risk of illness rather than a risk of diagnosis (illness plus precancerous forms).

The prevalence estimates were of great interest. In line with the expectations, the estimates of the time trends over a period of as much as 45 years provided an impressive picture of the growth of the population of breast cancer and prostate cancer survivors on a regional basis. The number of women with a history of breast cancer rose from 4,000 cases in 1970 to 52,700 in 2015. The number of prostate cancer patients increased from 1,900 cases in 1970 to 32,100 in 2015. Among males, but not females, an important finding was that the prevalence of lung cancer is expected to level off after 2010. The prevalence of colorectal cancer is still increasing in both sexes.

Table 1 - Emilia-Romagna population, proportion of the elderly population in 2010 and cancer registries with their coverage and beginning of registration

		Population	Population ≥65 years of age %	Coverage %	First year of incidence
Region	Emilia-Romagna	4,395,569	22.4	71.1	1978
Registry	Parma	437,349	22.5	100	1978
	Reggio-Emilia	525,267	19.7	100	1996
	Modena	694,579	20.8	100	1988
	Ferrara	358,972	25.5	100	1991
	Romagna*	1,107,057	22.3	100	1986

*The health care district of Imola is not included.

Table 2A - Estimated incidence, mortality and prevalence by cancer site for the year 2012 in Emilia-Romagna. 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	3,661	172.3	96.4	632	29.8	13.9	28,977	1,363.6
Stomach	728	38.9	21.3	470	25.1	13.1	4,014	214.3
Colon-rectum	2,939	157.0	83.8	984	52.6	26.7	18,853	1,006.8
Lung	1,967	104.9	55.7	1,647	87.8	45.3	5,386	287.1
Melanoma	529	28.3	19.3	54	2.9	1.7	4,924	263.0

Table 2B - Estimated incidence, mortality and prevalence by cancer site for the year 2012 in Emilia-Romagna. 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	3,459	174.1	103.3	805	40.5	17.6	49,759	2,505.3
Stomach	545	27.4	11.2	351	17.7	6.7	3,348	168.6
Colon-rectum	2,071	104.3	42.7	713	35.9	13.4	16,098	810.6
Lung	1,022	51.5	25.8	731	36.8	17.3	2,758	138.9
Melanoma	535	26.9	19.5	48	2.4	1.2	6,851	345.1
Cervix	141	7.1	5.2	56	2.8	1.6	1,638*	82.8*

*Limited-duration prevalence at 15 years.
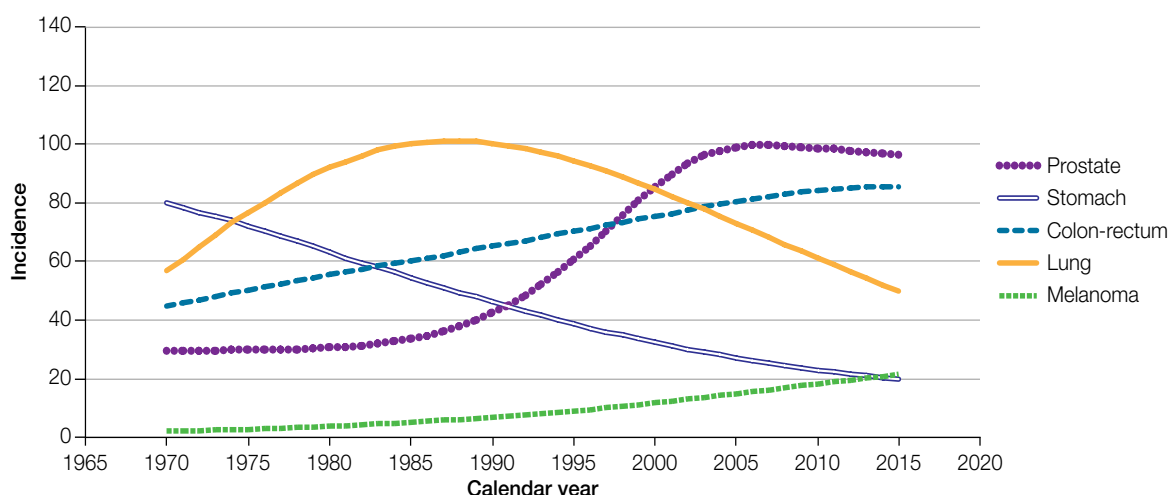
Figure 1 - Incidence estimates by cancer site in Emilia-Romagna in the period 1970-2015. Age-standardized rates (European population) per 100,000 person-years. Age 0-99 years, men.
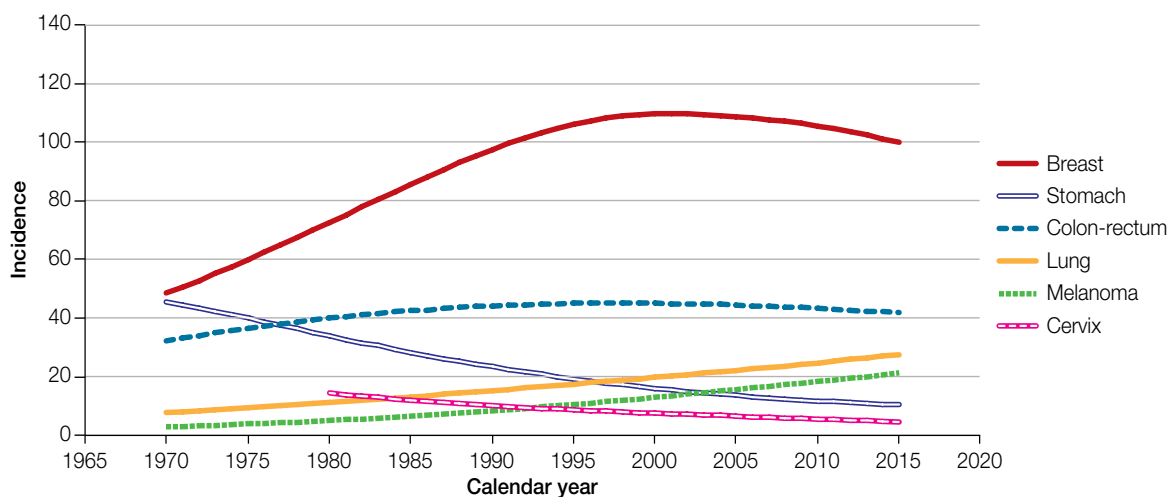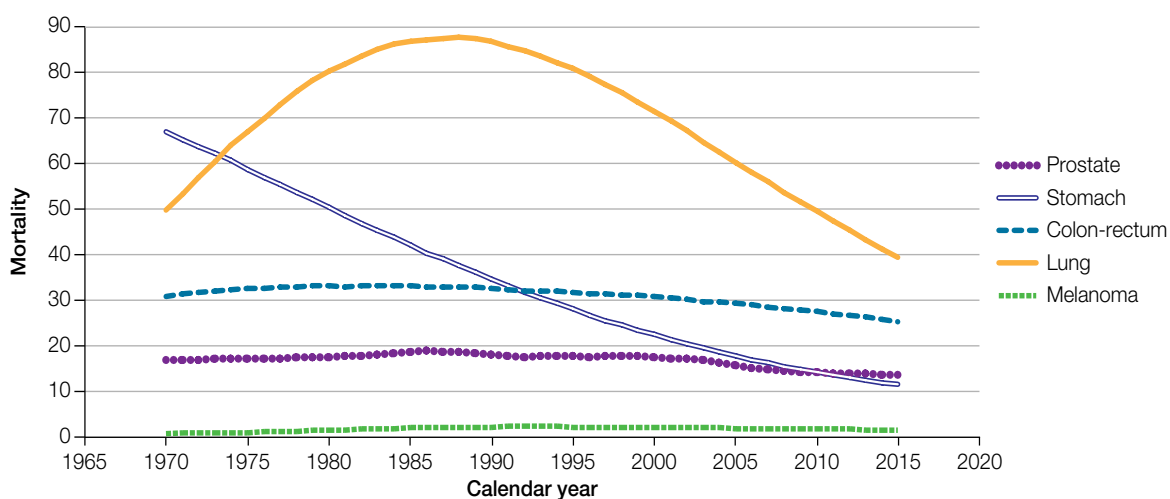

Figure 2 - Incidence estimates by cancer site in Emilia-Romagna in the period 1970-2015. Age-standardized rates (European population) per 100,000 person-years. Age 0-99 years, women.

Figure 3 - Mortality estimates by cancer site in Emilia-Romagna in the period 1970-2015. Age-standardized rates (European population) per 100,000 person-years. Age 0-99 years, men.
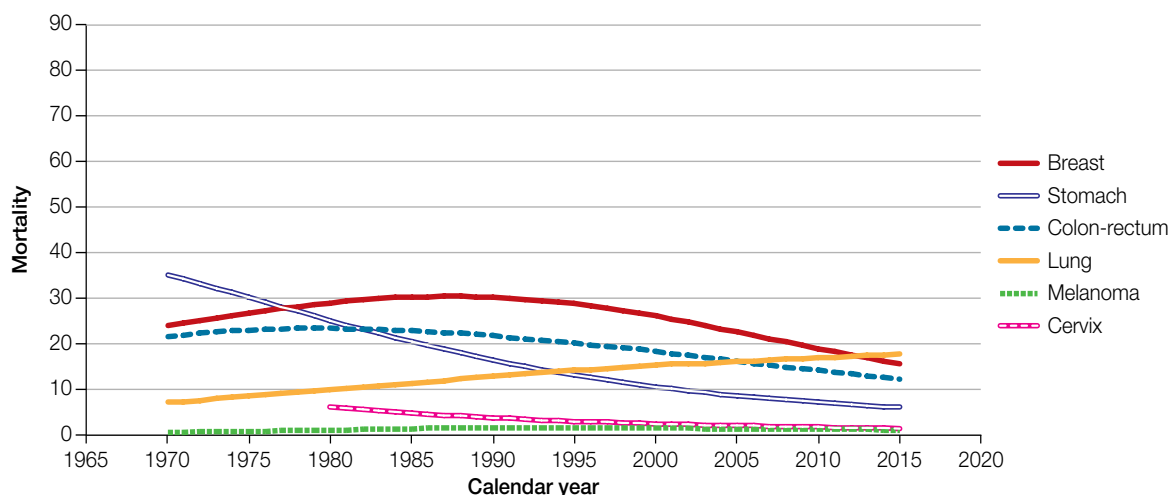
Figure 4 - Mortality estimates by cancer site in Emilia-Romagna in the period 1970-2015. Age-standardized rates (European population) per 100,000 person-years. Age 0-99 years, women.
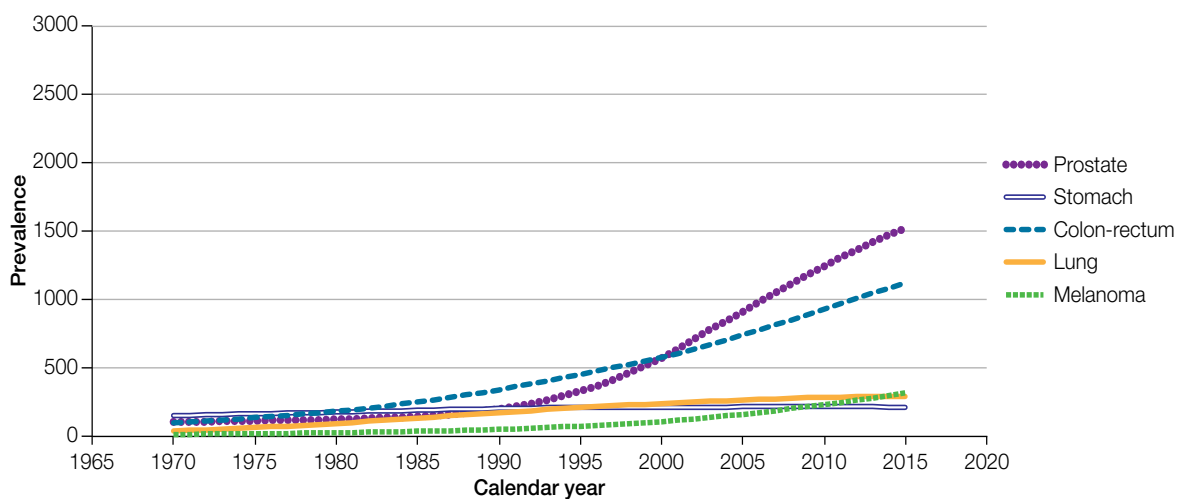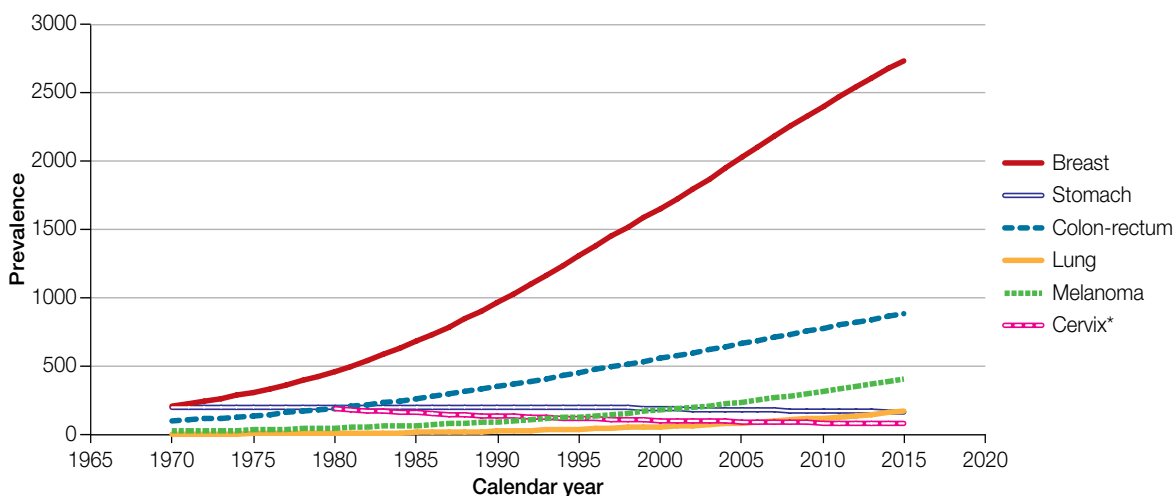

Figure 5 - Prevalence estimates by cancer site in Emilia-Romagna in the period 1970-2015. Crude proportion per 100,000 persons. Age 0-99 years, men.

*limited-duration prevalence at 15 years

Figure 6 - Prevalence estimates by cancer site in Emilia-Romagna 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. Il Sistema Informativo Politiche per la Salute e Politiche Sociali. https://siseps.regione.emilia-romagna.it/flussi – (Strutture dell'offerta ospedaliera: posti letto) (accessed 8 March 2013).

3. Facts and figures of the Regional Health Service of Emilia-Romagna (2007) – Servizio Sanitario Regionale Emilia-Romagna, pp 36-37. http://www.saluter.it/documentazione/rapporti/ssr/ssr_eng_maggio2009.pdf/view (accessed 8 March 2013).

4. Ferretti S, Finarelli AC: I tumori in Emilia Romagna, anno 2007. Collana "Contributi", a cura della Regione Emilia-Romagna. http://www.saluter.it/documentazione/rapporti/contributi/67-tumori/view (accessed 8 March 2013).

5. ISTAT: Statistiche sulle cause di morte anno 2008. http://www.istat.it/dati/dataset/20110412_00/ (accessed 8 March 2013).

6. Capocaccia R, Gavin A, Hakulinen T, Lutz JM, Sant M: Survival of cancer patients in Europe, 1995-2002: the EUROCARE-4 study. Eur J Cancer, 45: 901-908, 2009.

7. 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.

8. 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.

9. 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.

10. World Health Organization: International classification of diseases, 9th ed, WHO, Geneva, 1997.

11. 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.

12. 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.

13. Verdecchia A, De Angelis G, Capocaccia R: Estimation and projections of cancer prevalence from cancer registry data. Stat Med, 21: 3511-3526, 2002.