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Cancer estimates up to 2015 in Friuli Venezia Giulia

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ABSTRACT

Aims and background. This analysis intended to estimate the incidence, mortality and prevalence time trends for the major cancer sites up to 2015 in the Friuli Venezia Giulia region, northeastern Italy, where a population-based cancer registry has been covering the whole area since 1995.

Methods. The MIAMOD method, a statistical back-calculation approach, was applied to estimate incidence, mortality and prevalence figures, in the period 1970-2015, using mortality data from the Italian National Institute of Statistics and relative survival data from Italian cancer registries.

Results. We estimated that the cancer sites with the highest incidence rates in the forthcoming years will be breast in women (with an age-standardized incidence rate of 130 per 100,000 in 2015), prostate in men (97 per 100,000) and colon-rectum in both sexes (85 and 42 per 100,000 in men and women, respectively). The incidence rates for lung cancer will continue to decrease only in men (down to 43 per 100,000 in 2015). Although the decline in the mortality rates of lung, breast and colorectal cancers is likely to persist, these tumors will remain the big killers in the near future. The number of people living in Friuli Venezia Giulia after a cancer diagnosis is expected to continue to rise in particular for breast cancer (with a crude prevalence of 3,000 per 100,000 women in 2015), prostate cancer (1,700 per 100,000 men) and colorectal cancer (1,100 and 800 per 100,000 in men and women, respectively).

Conclusion. These estimates confirmed the epidemiological patterns in time trends of major cancer sites recorded in Friuli Venezia Giulia. They highlighted in particular the increasing number of people living after a cancer diagnosis as a result of population aging, earlier diagnosis and better prognosis, which warrants adequate public health policies.

Key words: cancer, cancer registries, incidence, prevalence, mortality, Friuli Venezia Giulia, regression analysis.

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Introduction

Located in the northeastern part of Italy, the Friuli Venezia Giulia (FVG) region counts approximately 1.2 million inhabitants. The proportion of elderly people in this region has been historically among the highest in Italy (23.4% of the population aged 65 years or more in 2010)[1], resulting in a strong impact of the cancer burden on the regional health care system. A population-based cancer registry has been registering all incident cases diagnosed in people living in the whole region since 1995[2]. Given the long process of data reviewing required to obtain high standards in terms of completeness and quality, the last available year of cancer registration in FVG, as of 2012, was 2007. Further updated data and projections for future incidence, mortality and prevalence of the major cancer sites are needed for a better quantification of the care and therapeutic needs in oncology and the appropriate planning of health programs. The objective of this statistical analysis was to provide, for the FVG region, estimates of the incidence and mortality rates and prevalence proportions for cancer of the lung, breast, prostate, colon-rectum, stomach, cervix and melanoma of the skin for the year 2012 and time trends up to 2015.

Material and methods

The MIAMOD method, as described elsewhere in detail[3,4], was applied to estimate the absolute number of incident cases, deaths and prevalent cases, crude and age-standardized (based on 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, MIAMOD 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)[5]. Specific mortality data for the years 2003, 2006, and 2007 were used to validate the 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[6]. The survival estimates for the northeastern macro area were assigned to FVG for all cancer sites except stomach and colon-rectum in women and lung in men, for which the region-specific survival was applied because of substantial differences compared with the overall survival in the northeastern 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), which allowed to make a distinction between cervix uteri, corpus uteri and uterus not otherwise specified (NOS). Unfortunately, the official mortality statistics for cervical cancer are undersized due to the misclassification of cancer of the uterus NOS. For this reason, the estimates for this site were performed after adjustment for such misclassification, using the method proposed by Capocaccia *et al.*[7], 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 in time trends as suggested by the most recent cancer registry data[8]. Mortality estimation up to 2010 was preliminarily performed by means of the PIAMOD method[9] so as to complete the missing mortality time series in the years 2004 and 2005 [5] 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 (APC) of the incidence and mortality rates estimated for the period 2001-2002.

Results

Estimates of selected cancer sites burden in FVG for 2012 are reported in Table 1. Among men, the most frequent incident cancers were prostate and colorectal cancer (with more than 1,000 and 800 new diagnoses, respectively), followed by lung cancer (approximately 500 cases), stomach cancer and melanoma (approximately 200 cases each). In women, breast cancer was by far the most common cancer site (with more than 1,200 estimated new diagnoses), followed by colorectal cancer (nearly 600 cases) and lung cancer (267 cases). Other cancers had a much smaller impact. The highest crude mortality rates in 2012 were estimated in men for lung and colorectal cancer (77 and 49 per 100,000, respectively) and in women for breast, colorectal and lung cancer (48, 39 and 33 per 100,000, respectively). It was estimated that in 2012 more than 16,000 women in FVG were living with a previous diagnosis of breast cancer, 9,000 men with a diagnosis of prostate cancer, and approximately 9,700 people with a diagnosis of colorectal cancer.

The time trends are shown in the figures: age-standardized incidence rates (Figures 1 and 2), age-standardized mortality rates (Figures 3 and 4), and crude complete prevalence proportions (Figures 5 and 6). The main results are grouped by cancer site and summarized below.

Breast

The upward incidence trend estimated from the 1970s onwards for breast cancer was expected to continue, but to a lesser extent, up to 130 per 100,000 in 2015, with corresponding APCs ranging from 2-3% until 1993 to approximately 0.6% in the 2000s. The mortality rates were estimated to keep decreasing as already seen from the early 1990s (from 33 to 19 per 100,000 in 2015). Conversely, prevalence was expected to rise steadily in the near future (up to nearly 3,000 per 100,000 in 2015).

Prostate

For prostate cancer, the estimated incidence rates were increasing until 2005 (around 107 per 100,000/year) and declining thereafter (97 per 100,000 in 2015). These estimates were lower than the incidence rates observed by the FVG cancer registry[2] (see Appen-

dix). The mortality rate projections showed a declining trend (from 24 per 100,000/year in the late 1980s to 14 per 100,000 in 2015). As a result, the prevalence was expected to rise sharply in the forthcoming years (up to 1,700 per 100,000 in 2015).

Colon and rectum

The estimated incidence rates for colorectal cancer among men were rising (up to 85 per 100,000 in 2015), though to a lesser extent than in the period up to the mid 1990s. In women the incidence rates were estimated to remain much lower than in men and to be almost stable (around 42 per 100,000/year). Slight differences emerged between these estimates and the data observed by the FVG cancer registry[2] (see Appendix). Mortality rate projections for colorectal cancer showed a persisting downward trend in both sexes (down to 25 and 14 per 100,000 in men and women, respectively, in 2015). Conversely, the prevalence proportions were estimated to rise (up to 1,100 and nearly 800 per 100,000 in men and women, respectively, in 2015).

Lung

In the male population, the sharp decline in lung cancer incidence rates seen from the mid 1980s was expected to persist (down to 43 per 100,000 in 2015). Conversely, the incidence rates in women were estimated to continue to rise slightly (from 20 to 22 per 100,000 in 2000 and 2015, respectively). The mortality trends were very similar to the incidence trends. Prevalence, although one of the lowest among the considered cancers, was estimated to be gradually rising in the near future (up to 225 and 150 per 100,000 in men and women, respectively, in 2015).

Stomach

The downward incidence trend of gastric cancer was estimated to persist in both sexes in the forthcoming years (down to 21 and 7 per 100,000 in men and women, respectively, in 2015). The mortality rates strictly reflected the incidence rates and were expected to decline steadily in the future (down to 13 and 4 per 100,000 in men and women, respectively, in 2015). Prevalence was expected to remain low but slightly increasing among men (220 and 120 per 100,000 in men and women in 2015, respectively).

Skin melanoma

Melanoma incidence rates were estimated to increase steadily in men throughout the study period (up to 25 per 100,000 in 2015), whereas they were estimated to remain stable at the level of the mid 1990s in women (around 13 per 100,000/year). The mortality rates, which were very low for both genders, were expected to decrease (down to 2 and 0.7 per 100,000 in men and women, respectively, in 2015). A sharp rise in prevalence was expected in the near future (up to roughly 400 cases per 100,000 in both sexes in 2015).

Cervix uteri

During the study period the cervical cancer incidence and mortality rates were constantly decreasing (from 15 and 7 per 100,000 in 1980 to 7 and 2 per 100,000 in 2015, respectively). The prevalence was also expected to slightly decrease in the future (down to 98 cases per 100,000 in 2015).

Discussion

The estimates herein provided, though not comprehensive of all tumor sites and types, give an indication of the cancer burden in the FVG region from 1970 up to 2015. The study findings indicate that breast, colon-rectum and prostate will be the cancer sites with the highest incidence rates in the forthcoming years. Conversely, the incidence of lung cancer, which was by far the most frequent cancer in men till the early 1990s, will continue to decline in men. The mortality estimates show downward trends for all the considered cancers. Although the decline in mortality for lung, breast and colorectal cancer is likely to persist, these cancers will remain the big killers in the near future. As a result of earlier diagnosis and/or better prognosis in addition to population aging, the number of people living after a cancer diagnosis is estimated to rise, in particular for breast, prostate and colorectal cancer. A recent estimation of the cancer burden including all cancer types reported that around 58,000 people were living in FVG region in 2006 with a previous diagnosis of any cancer and estimated a 3-5% increase in prevalence per year[10].

The presence in FVG of a population-based cancer registry covering the whole region offers the possibility – rare in Italy – of comparing estimated and observed incidence data in the period 1995-2007. The comparison revealed good agreement for the examined cancer sites, except for prostate and colorectal cancer in men[2] (see Appendix).

The FVG cancer registry reported a much higher increase in incidence rates for prostate cancer (up to more than 130 per 100,000 in 2007, APC = +2.6% between 1998 and 2007) compared with the MIAMOD estimates, and no signs of rate reductions. This could be explained taking into consideration that the MIAMOD estimates are based on mortality rates that, for prostate cancer, were not so heavily modified by the introduction of the prostate-specific antigen (PSA) blood testing as the incidence rates were. The spread of PSA testing started at the end of the 1980s, but it was between 1998 and 2009 that the total number of PSA tests almost doubled in FVG[11]. The huge increase in incidence rates in the same period was not accompanied by a corresponding increase in mortality, which was almost stable or slightly declining from the late 1980s, thus pointing to a potentially elevated rate of overdiagnosis (i.e. cancers that would not have been diagnosed in the absence of screening) in FVG. It has been estimated that 23-42% of prostate cancer cases in the United States result from over-

diagnosis due to PSA testing[12] and that overdiagnosis accounted for 66% of screen-detected tumors in the European setting[13].

With regard to colorectal cancer, our estimates were consistent with the observed data of the FVG cancer registry only up to 2001; after that year, the model projections foresaw a continuously upward incidence trend in males, whereas the latest registry data revealed a leveling off of the incidence after 2005 to around 70 per 100,000/year[2]. We can reasonably exclude that the difference between the estimated and observed data was attributable to opportunistic screening activities, which were not common in FVG: in fact, according to the PASSI survey of 2007 in FVG, only 24% of people aged 50-69 years said they had had a colonoscopy or fecal occult blood test (FOBT) in the recommended interval[14]. Furthermore, as a result of the activation of regional organized screening in 2008 (with biannual FOBT being offered every 2 years to people aged 50-69 years) the incidence of colorectal cancer would probably have risen during the first round of screening and fallen thereafter.

Also the breast cancer incidence projections, which showed a persisting upward trend, should be considered cautiously. These figures could be affected more by the impact of early diagnosis than of the natural evolution of the disease. However, comparison of the estimates with the observed data from the FVG cancer registry in the period 1995-2007[2] (see Appendix) showed a good agreement, except for the incidence peak registered in 2006 as a result of the high adherence to organized screening – biannual mammograms offered to women aged 50-69 years – from its activation in December 2005[15]. Nevertheless, opportunistic screening was also widespread in FVG before 2006: according to regional data[15] the percentage of women aged 50-69 who had a mammogram in the previous 2 years rose from 35% in 2004-2005 to 76% in 2008-2009, and, according to an ISTAT survey[16], the percentage of women of the same age having had at least 1 mammogram in their lifetime increased from 66% to 78% between 1999-2000 and 2004-2005.

The declining trend observed for the cervical cancer incidence and mortality also largely reflects the effect of screening activities. These were widespread among women living in FVG even before the introduction of the organized program in 1999 consisting of a Papanicolau (Pap) smear offered every third year to women aged 25-64 years. The percentage of women aged 25-64 years who had a Pap smear in the previous 3 years rose from 40% in the period 1996-1998 to 66% in 2008-2010[15] and the percentage of women of the same age having had at least 1 Pap smear in their lifetime increased from 80% to 86% between 1999-2000 and 2004-2005[16]. The projections up to 2015 included in this paper are not expected to be affected by the impact of HPV immunization, as the FVG region started to offer the vaccine free of charge to girls between 11 and 16 years of age in 2008 and voluntary vaccination of older women is very uncommon. However, future estimates must take it seriously into account, as some effect of HPV immunization in reducing the cervical cancer incidence rates is likely to emerge in the next 20-30 years.

Prevalence estimates and projections must be taken with caution as they are particularly sensitive to incidence and survival time series produced many decades earlier for which few or no observed data are available to check the considered models. We compared the MIAMOD prevalence estimates with those provided only for 2006 by AIRTUM (computed using incidence and survival data from cancer registries)[10]. The estimates showed good agreement (difference <10%) for stomach cancer (162 per 100,000 according to MIAMOD *vs* 157 according to AIRTUM), colorectal cancer (694 *vs* 634) and breast cancer (2,289 *vs* 2,209). Conversely, considerable differences emerged for lung cancer (153 *vs* 136), prostate cancer (1,080 *vs* 1,261) and melanoma (233 *vs* 190 for men and 299 *vs* 250 for women). For cervical cancer, the extrapolation in the past of the decreasing trend estimated during the 1980s and 1990s may have inflated the past incidence level and consequently the estimated prevalence proportions. Therefore, for cervical cancer we reported here only the 15-year limited-duration prevalence proportion. This was in good agreement with the AIRTUM estimates for 2006 (99 and 96 per 100,000, respectively).

Estimates are always prone to limitations and, as already highlighted in this paper, the projections for tumors involved in screening should be considered with caution. The MIAMOD estimates were based on mortality data up to 2002, which could only partially reflect the effect of recent screening activities. However, the major limitation of the present study is the absence of estimates for several important cancer sites/types. In particular, estimation for hematopoietic neoplasms, which also have a strong impact on the health care system, are not feasible using the MIAMOD method as it is based on mortality data, which are not very reliable for such neoplasms.

In conclusion, monitoring indicators of the cancer burden through the joint use of data from the FVG cancer registry, which are more accurate and comprehensive of all cancer sites, and data from estimates, which are more updated and allow future projections, can be crucial for setting priorities among possible health system activities in a limited-resource setting. In a future perspective, given the very few therapeutic options for lung cancer, primary prevention through tobacco control will be still the priority, especially among women. Promoting compliance with organized screening programs as well as guaranteeing adequate treatment and follow-up will remain the main goals for reducing the colorectal and breast cancer burden. Conversely, the indiscriminate use of PSA testing should be discouraged in order to avoid overdiagnosis and overtreatment for prostate cancer. Lastly, the implications in terms of the public health burden of the increasing number of people living after a cancer diagnosis warrants adequate health policies.

Table 1 - Incidence, mortality and prevalence estimates by sex and cancer site for the year 2012 in Friuli Venezia Giulia. Number of cases and deaths, crude and age-standardized rates (European population) per 100,000 person-years and crude prevalence proportion per 100,000 persons. Age 0-99 years

Sex / 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
Male								
Prostate	1,082	180.9	101.4	176	29.4	14.5	9,086	1,518.9
Stomach	218	39.7	22.7	138	25.2	13.9	1,170	212.9
Colon-rectum	806	146.7	84.2	268	48.8	26.7	5,440	990.0
Lung	493	89.6	49.9	424	77.2	42.0	1,241	225.5
Melanoma	196	35.8	23.4	21	3.8	2.2	1,875	341.4
Female								
Breast	1,243	213.1	129.1	278	47.6	20.6	16,344	2,803.5
Stomach	119	20.4	7.8	81	13.8	5.1	716	122.9
Colon-rectum	578	99.2	42.0	229	39.2	15.1	4,233	726.4
Lung	267	45.8	21.6	195	33.4	14.9	762	130.8
Melanoma	107	18.3	13.7	11	1.8	0.9	2,089	358.6
Cervix	53	9.1	7.2	19	3.3	2.0	566*	97.4*

*Limited-duration prevalence at 15 years.

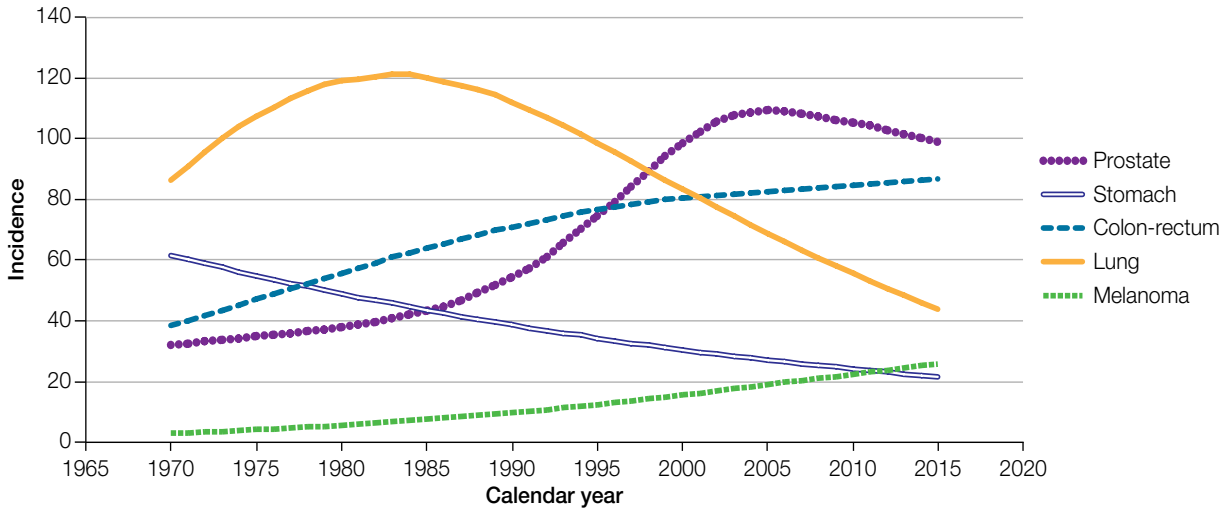


Figure 1 - Incidence estimates by cancer site in Friuli Venezia Giulia in the period 1970-2015. Age-standardized rates (European population) per 100,000 person-years. Age 0-99 years, men.

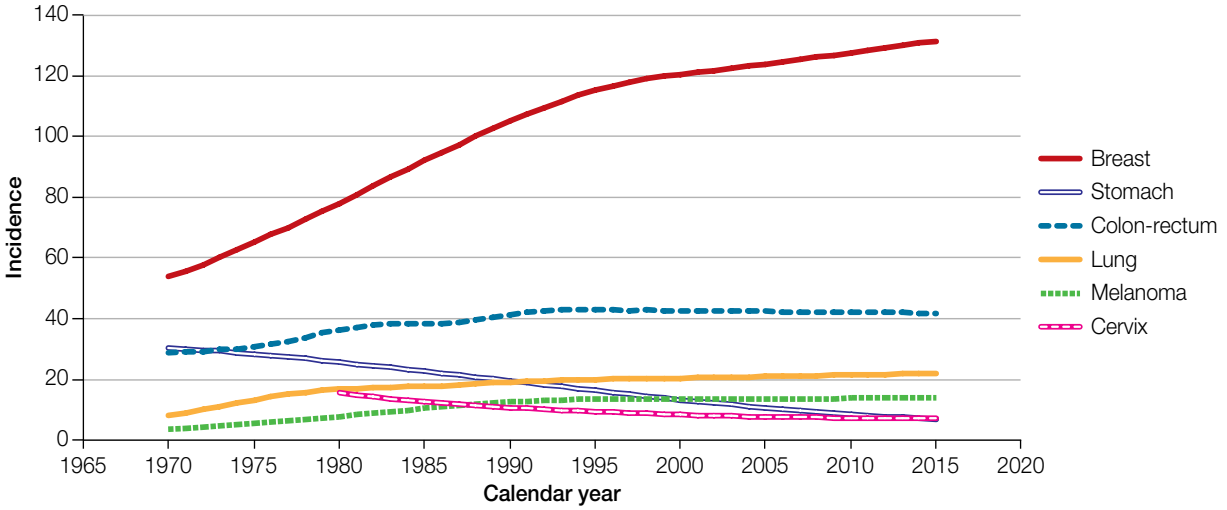


Figure 2 - Incidence estimates by cancer site in Friuli Venezia Giulia in the period 1970-2015. Age-standardized rates (European population) per 100,000 person-years. Age 0-99 years, women.

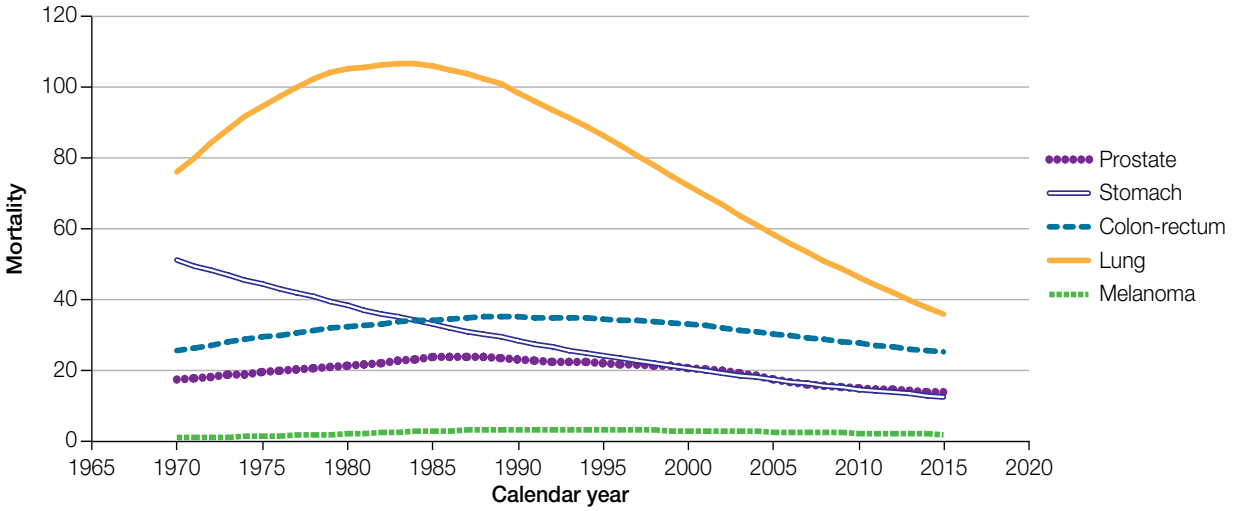


Figure 3 - Mortality estimates by cancer site in Friuli Venezia Giulia in the period 1970-2015. Age-standardized rates (European population) per 100,000 person-years. Age 0-99 years, men.

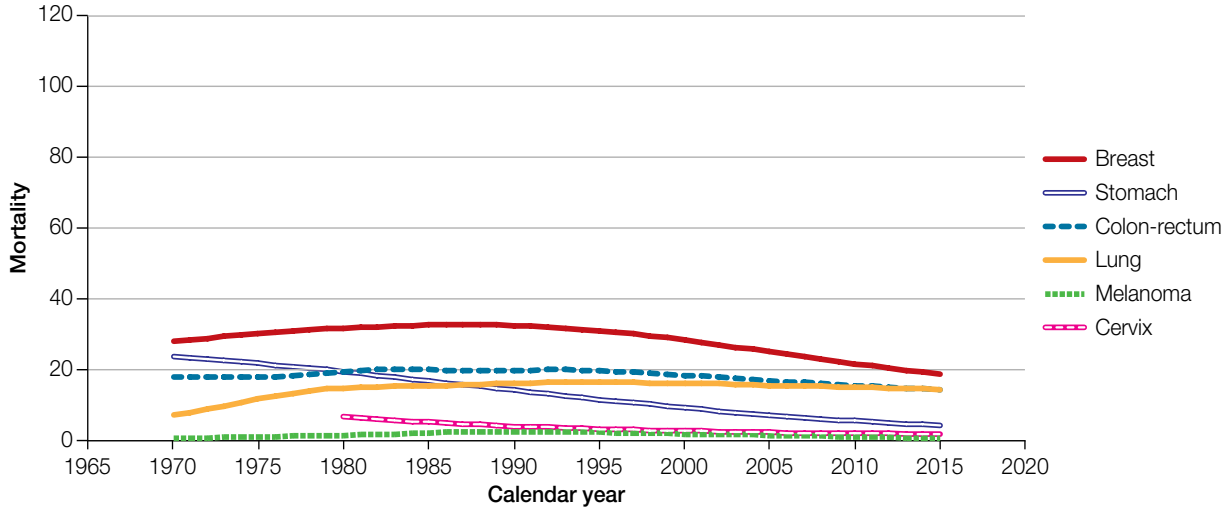


Figure 4 - Mortality estimates by cancer site in Friuli Venezia Giulia in the period 1970-2015. Age-standardized rates (European population) per 100,000 person-years. Age 0-99 years, women.

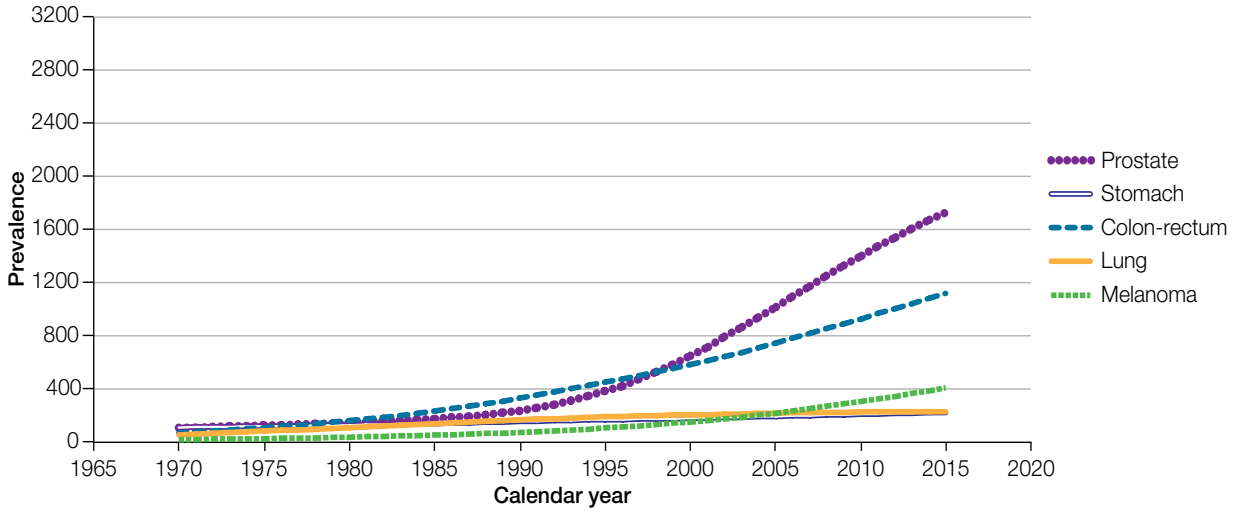
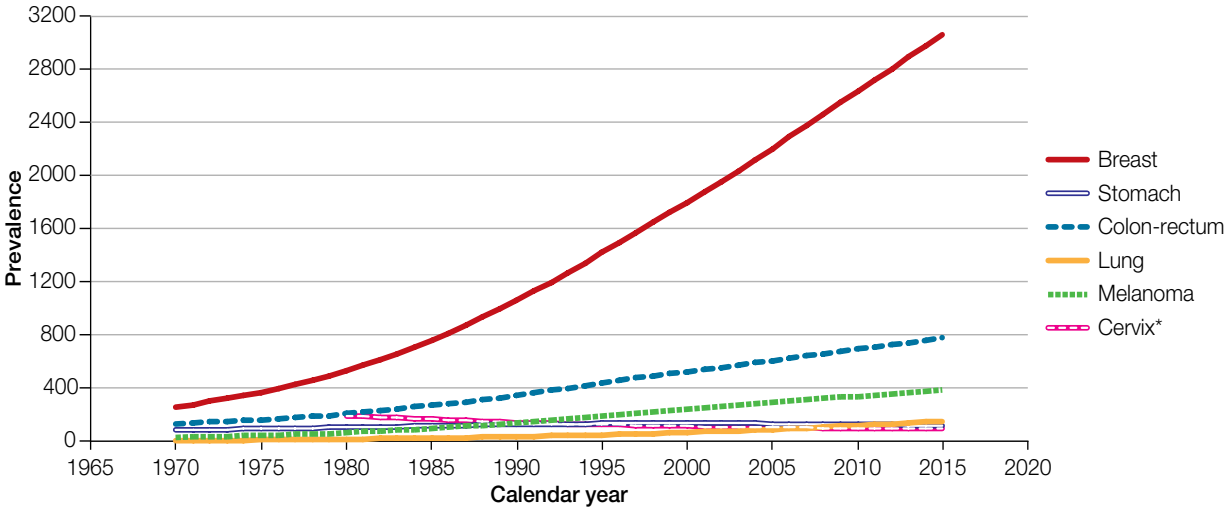


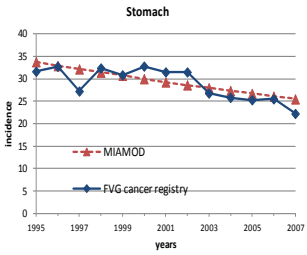
Figure 5 - Prevalence estimates by cancer site in Friuli Venezia Giulia in the period 1970-2015. Crude proportion per 100,000 persons. Age 0-99 years, men.

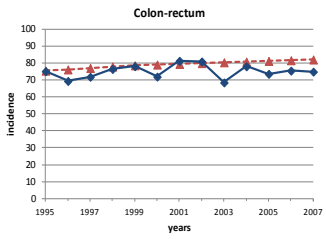


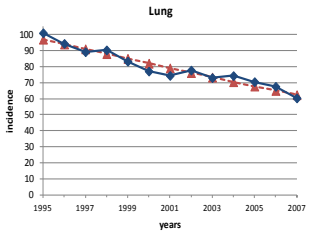
limited-duration prevalence at 15 years

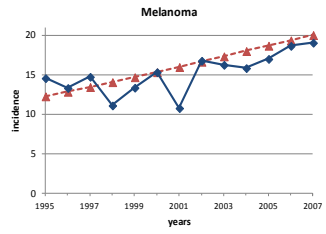
Figure 6 - Prevalence estimates by cancer site in Friuli Venezia Giulia in the period 1970-2015. Crude proportion per 100,000 persons. Age 0-99 years, women.

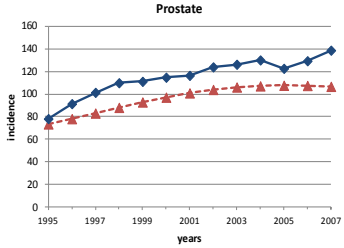
Males



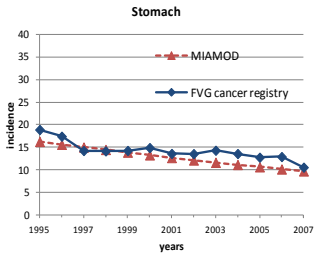


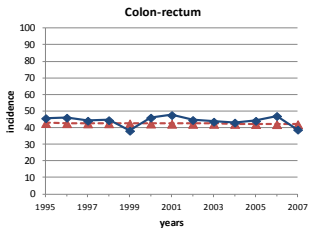


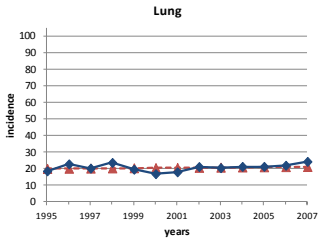


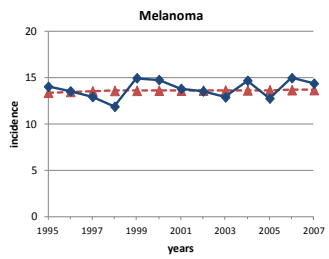


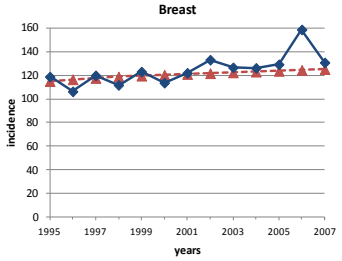
Females

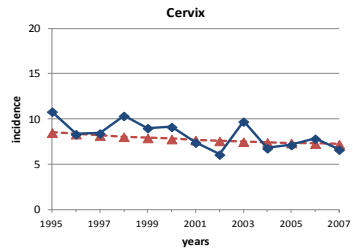












APPENDIX: Incidence rates estimated by MIAMOD (dotted line) and observed by Friuli Venezia Giulia (FVG) cancer registry (solid line) in the period 1995-2007. Age-standardized rates (European population) per 100,000 person-years by sex and cancer site.

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