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Estimates of cancer burden in Piedmont and Aosta Valley

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ABSTRACT

Aims and background. Cancer registration in Piedmont currently covers the city of Turin and the province of Biella, together representing 24% of the regional population. The objective of this paper is to provide estimates of the incidence and mortality rates and prevalence proportions for cancer of the lung, breast, cervix, prostate, colon-rectum and stomach and melanoma of the skin for 2012 and the time trends up to 2015 for the Piedmont and Aosta Valley regions.

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. The MIAMOD estimates were also compared with those obtained by applying a method based on the mortality-incidence and prevalence-incidence ratios.

Results. The most frequently diagnosed cancers in absolute terms were prostate, colorectal, breast and lung cancer with about 5,000, 4,700, 3,300, and 2,900 new cases, respectively, in 2012. Incidence rates were rising for melanoma in both sexes and lung cancer in women, while they diminished for cervical and stomach cancer. For prostate cancer and male lung cancer the rates initially increased but were estimated to decrease in the most recent period. Colorectal cancer also increased up to the 1990s but was estimated to reach a plateau in the final years of estimation. Prevalence increased for all the considered cancers with the exception of cervical cancer. Mortality was declining for all considered cancers with the exception of lung cancer in women.

Conclusions. Monitoring indicators of the cancer burden is crucial for setting priorities among possible health system activities in a limited-resource setting. Piedmont has long invested in organized, population-based screening programs: these will have to be extended and accompanied by greater efforts in primary prevention.

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

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Introduction

Piedmont is a region located in the northwestern part of Italy with a population of approximately 4.45 million at the beginning of 2011[1]. The name Piedmont comes from medieval Latin Pedemontis, i.e. *ad pedem montium*, meaning "at the foot of the mountains". Its economy is based on agriculture, with Piedmont being one of the largest wine-growing regions in Italy, as well as industrial centers, most importantly Turin, home to the car industry. Since the beginning of the last century Piedmont's economic vitality attracted and still attracts migrants from other Italian regions and now also from other countries, contributing to the variegated makeup of its population. Twenty-three percent of the population is 65 years of age or older, and the birthrate is decreasing (8.5 newborns per 1,000 inhabitants in 2011)[1].

With more than 100,000 hospital admissions for cancer each year (13.5% of total admissions), care is provided through a network of oncology centers including the Aosta Valley region, with 5 "oncology hubs" where specialist care to cancer patients is delivered by a multidisciplinary approach[2].

Started in 1992 as an intervention/evaluation study in Turin, population-based organized screening for breast, cervix and colorectal cancer is now offered to the target population of the whole region.

At present, cancer registration covers the city of Turin (about 907,000 inhabitants in 2011) and the province of Biella (185,000), amounting to 24% of the regional population. Observed data by cancer registries are usually 2 or 3 years behind: for Turin the last available data of cancer registration pertained to 2009 while for Biella this was 2007[3]. Estimates of the principal epidemiological indicators (incidence, mortality and prevalence) for the whole region and projections to future years are needed for the appropriate planning of health programs and the allocation of resources within the Piedmont Oncology Network.

The objective of this paper is to make available for the whole Piedmont region and Aosta Valley estimates of incidence and mortality rates and prevalence proportions for cancers of the lung, breast, cervix, prostate, colon-rectum, stomach, and melanoma of the skin for 2012 and time trends up to 2015.

Material and methods

The MIAMOD method[4] was applied to estimate the absolute number of incident cases, deaths and prevalent cases, crude and age-standardized (using the standard European population) incidence and mortality rates (per 100,000 person-years), and prevalence proportions (per 100,000) for the period 1970-2015. The 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 estimation was based on mortality data derived from the Italian National Institute of Statistics (ISTAT) for the period 1970-2002[5] with cause of death coded according to the ninth revision of the International Classification of Diseases (ICD-9)[6], and relative survival estimates. Additional mortality data for the years 2003, 2006 and 2007 (data for 2004-2005 were not yet published by ISTAT) were used to validate the expected mortality projections. Survival estimates were obtained 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 for the period 1985-2002[7]. The geographical area and the age of patients were considered as categorical covariates in the survival model. The covariate year of diagnosis was modeled for each site and sex as continuous or categorical and as unique for all areas or variable by area according to the pattern of observed survival data. The survival estimates for the northwestern macro area were assigned to Piedmont for all cancer sites. 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 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. Estimates of cervical cancer were particularly difficult to compare because of the poor specification of uterine cancer subsites in death certificates. Therefore, a specific methodology[8,9] allowing to correct mortality data provided by official statistics that were flawed by misclassification with uterus not otherwise specified (NOS) was used for cervical cancer. This methodology can be applied from 1980 onwards because before that date 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 cervical 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. For cervical cancer, 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.

A specific procedure for prostate cancer was used to capture recent trends. Mortality estimation up to 2010 was preliminarily performed by means of the PIAMOD method[10] in order to complete the mortality time series in the missing years 2004 and 2005, and to base the 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.

The estimates of age-specific incidence and mortality for melanoma were obtained by linearly projecting the age-specific annual percent change of the incidence and mortality rates estimated for the period 2001-2002. The total rates were obtained by age-specific rates. The age-standardized rates are based on the standard European population.

The Piedmont Cancer Registry was also asked by the Piedmont Oncology Network to provide subregional estimates and projections of the cancer burden for the reference local areas. Since the policies for resource allocation in cancer care were defined after negotiations with the local governments, subregional estimates were seen as the optimal basis for taking informed decisions.

Subregional estimates were obtained applying a different method based on the mortality-incidence ratio (MI), after projecting mortality trends based on age-cohort models and applying the MI ratio observed in the cancer registries of the Northwest of Italy in order to increase the statistical stability of this index[11]. Furthermore, the prevalence-incidence ratio calculated from the registry data was applied to the estimated incidence in the regional or subregional populations. This method is less sensitive to specific parametric assumptions and user choices – especially regarding survival trends – inherent in the modeling approach applied in MIAMOD. On the other hand, it is intrinsically biased because it uses the information (mortality) from a previous cohort of patients, with different patterns of diagnosis, treatment and care (and thus potentially different survival) than patients diagnosed more recently (incident cases). This paper will also compare estimates obtained with the 2 methods independently applied by 2 separate teams of statisticians to a real case.

Results

Table 1 presents a summary of the demographic characteristics of Piedmont and its areas covered by cancer registration. The total proportion of coverage was 24% in 2011. Tables 2A and 2B present the cancer burden estimated for the year 2012 in Piedmont and Aosta Valley, separately for men and women. Among men, prostate cancer brought the highest burden in terms of incidence and, thanks to its good prognosis, prevalence as well: almost 5,000 new cases were expected in 2012 in Piedmont and the Aosta Valley.

In the last 15-20 years lung cancer was the first incident cancer among men while, with 1,975 new cases, it is now the third after prostate cancer and colorectal cancer, the latter representing a higher burden with more than 2,600 new cases. However, given its poor prognosis, lung cancer will remain the leading cause of death among male cancer patients with about 1,700 deaths each year.

The most frequent cancers in women were breast, colorectal and lung cancer with about 3,200, 2,100 and 900 new cases, respectively, in 2012. However, the impact of these 3 cancer sites on mortality was almost equal: between 700 and 800 deaths for each cancer. This was the result of their very different prognosis, which is notoriously poor for lung cancer and much better for breast cancer, with survival now approaching 90% after 5 years of follow-up. As a result, about 50,000 women in 2012 were estimated to have had a diagnosis of breast cancer. For cervical cancer about 160 new cases and 70 deaths each year were estimated. Table 3 reports the comparison between estimates obtained by 2 different methods: MIAMOD and the MI ratio. The results showed good agreement in the case of prostate, stomach and lung cancer, with differences often below 5% and never above 10%. Estimates of the colorectal cancer incidence, mortality and prevalence showed the greatest differences (25%, 12% and 24%, respectively, in men) while in women the differences were less marked.

An advantage of the MIAMOD method is that it provides time projections to study the trends of the main epidemiological indicators. The time trends of age-standardized incidence and mortality and crude prevalence over the period 1970-2015 are shown in Figures 1 to 6 for both sexes. The principal findings are summarized below.

Breast

After a fast upward trend since the 1970s the breast cancer incidence was estimated to stabilize and then decline to about 90 new cases per 100,000 in 2015. The mortality rates were estimated to keep decreasing from the early 1990s onwards to less than 15 deaths per 100,000 in 2015. By contrast, prevalence was expected to rise steadily as a combined effect of stabilized incidence and decreased mortality.

Prostate

The incidence estimate for prostate cancer showed an initial stabilization and subsequent decline after 2005. Projections of the age-standardized mortality rates showed a slight but stable tendency to decline to fewer than 20 per 100,000 estimated deaths in 2015. The effect of a decline in prevalence, given the expected decline in incidence, was beyond the present projections' time limit.

Colon and rectum

After a period of constant increase until 2006 in men and earlier in women, the incidence of colorectal cancer entered a phase of stabilization, while the mortality showed a persisting downward trend in both sexes (down to 23 and 13 per 100,000 in men and women, respectively, in 2015). As a result of the opposite trends in incidence and mortality, its prevalence is still estimated to rise.

Lung

The sharp decline in the lung cancer incidence rates in men since the 1990s was expected to persist. By contrast, the incidence rates in women were estimated to increase slightly. The mortality trends were very similar to the incidence trends, with a slight divergence between the 2 indicators, particularly in women.

Stomach

The downward incidence trend of gastric cancer was estimated to persist in both sexes over the forthcoming years (down to about 13 and 7 new cases per 100,000 in men and women, respectively, in 2015). Mortality closely reflected the incidence rates and was expected to drop to about 8 and 4 deaths per 100,000 in men and women, respectively, in 2015. Prevalence was expected to remain low but increasing slightly up to 220 and 120 per 100,000 in men and women, respectively.

Skin melanoma

Melanoma was known as one of the rapidly increasing neoplasms. The model estimates produced incidence rates passing from a mere couple of new cases per 100,000 in 1970 to about 20 in 2015. However, recent observed data from the Piedmont Cancer Registry showed a possible stabilization of rates in recent years (2007-2009), while *in situ* melanoma showed a constantly and rapidly increasing trend. The mortality rates, which were very low for both sexes, were expected to decrease further.

Cervix uteri

With the warnings and cautions presented in the methods section when interpreting cervical cancer estimates, a persistent decrease in incidence was also supported by the observed data. The estimated mortality trends showed a sharp decrease from 8 per 100,000 in 1980 to about 2 per 100,000 in 2015. The 15-year prevalence was also decreasing.

Discussion

The intrinsic value of cancer burden estimates lies in their use for resource allocation and health care planning in areas not yet covered by cancer registration. Piedmont has pioneered in the field of estimates providing local, regional and national estimates since the late 1990s[12,13]. Indeed, these estimates were used for the planning of health care services in Piedmont, as in the case of instituting radiotherapy centers across the region[14], or the population-based screening programs[15].

The present analysis offers an updated picture of the cancer burden in the Piedmont and Aosta Valley regions combined in 2012 as well as projections up to 2015. As expected, the findings indicated that breast, colon-rectum, and prostate will be the cancer sites with the highest incidence rates in the forthcoming years. However, the most interesting findings are those related to projections of future trends. A group of cancers is consistently decreasing, including lung cancer in men, cervical cancer in women, and stomach cancer in both sexes; this is partially related to changes in lifestyles that occurred in the previous decades. By contrast, an increasing trend persisted until recently for lung cancer in women, after an epidemic that began well after that of men. A tendency for the incidence to stabilize was observed for colorectal cancer in both sexes and breast cancer where also a slight decline became visible after year 2005. For prostate cancer a possible reduction of its incidence and mortality was expected in the coming years. This could be explained considering that the spread of PSA testing, which started at the end of the 1980s, might have reached its peak in the early 2000s and then diminished, partly due to recent negative results of a meta-analysis showing that PSA screening did not significantly decrease the mortality of prostate cancer[16]. The combined effects of stable mortality and the recent stabilization of the observed incidence, with a direct effect on survival, can have influenced the estimates based both on the MIAMOD and MI ratio methods.

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 expected to rise. It was recently estimated that around 204,000 people were living in Piedmont in 2006 with a previous diagnosis of any cancer[17].

The results showing a reduction for breast cancer and a stabilization, or possibly an initial decrease, in colorectal cancer, can be the combined effect of the early start of population-based screening programs (early in the 1990s for breast cancer and later in the 1990s for colorectal cancer) in Piedmont and possibly a change in risk factors among populations. The effect on breast cancer screening is sustained by the presence of a prevalence round effect on the observed incidence, with an initial increase and a subsequent decline in rates[3], and by the high compliance with and coverage of the screening programs in Piedmont[18]. Furthermore, part of the projected decline in breast cancer has been suggested[19] to be related to the change in menopausal hormone replacement therapy after the results of the Women's Health Initiative study[20].

Estimated data are prone to limitations. In particular, projections for those tumors involved in screening should be considered with caution. All the recommended organized screening programs (i.e., for cancer of the uterine cervix, breast and colon-rectum) have been implemented in Piedmont on a regional level since the 1990s. In addition, estimates for cervical cancer are particularly problematic since the methods for estimating the part in mortality coded as uterus NOS is based on reproportioning the known proportion of specific mortality from cancer registry data. The choice of registry data is essential. Such proportions were derived from cancer registries data including Turin cancer registry[8].

The Piedmont Cancer Registry has also provided regional estimates at a more detailed geographical level, so fulfilling a specific interest and request by the regional governance for the local planning of resources[3]. We therefore had the opportunity to compare the estimated incidence, mortality and prevalence with estimates obtained with the MI ratio method. The comparison revealed good agreement for all cancer types except colorectal cancer and to a lesser extent (mostly limited to prevalence estimates) prostate and breast cancer. The reasons for the differences in prostate and breast cancer estimates can easily be found in the effect of using survival figures that are slightly inflated by the lead-time bias caused by earlier diagnosis as a result of organized or sporadic screening. Reasons for the differences in colorectal cancer estimates are more difficult to identify, since these could be due to a mix of the following factors: the effect of organized screening in Piedmont; reliability issues with specific mortality indicators, where attitudes in declaring this type of cancer death certification can vary across Italy[21]; and different assumptions regarding the survival trends in the period 2003-2015, estimated to keep increasing like in previous years according to MIAMOD but to be stabilizing according to the MI method.

In conclusion, monitoring indicators of the cancer burden through the joint use of data from the Piedmont Cancer Registry and data from estimates and projections can be crucial in setting priorities among possible health system activities in a limited-resource setting. Piedmont has long invested in organized, population-based screening programs: these have to be continued, extended and accompanied by greater efforts in primary prevention with initiatives towards promoting healthier lifestyles, quitting smoking and weight control.

Table 1 - Population of Piedmont and Aosta Valley, and cancer registration coverage

Region	Registry	Population 2011		Population ≥65 years of age (%)		Coverage %	First year of incidence
		Male	Female	Male	Female		
Aosta Valley		62,803	65,427	18.0	23.7	0%	
Piedmont		2,158,445	2,298,890	19.9	25.6	24%	1985
	Turin (City)	431,550	476,013	20.6	27.0	100%	1985
	Biella (Province)	88,844	96,924	21.5	28.8	100%	1995

Table 2A - Estimated incidence, mortality and prevalence by cancer site for the year 2012 in Piedmont and Aosta Valley. 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	4,884	219.6	122.4	776	34.9	17.5	38,725	1,741.1
Stomach	520	25.8	14.7	352	17.5	9.6	2,498	123.7
Colon-rectum	2,650	131.2	72.6	937	46.4	24.5	17,136	848.3
Lung	1,975	97.6	53.5	1,680	83.0	44.4	5,143	254.1
Melanoma	500	24.8	18.6	61	3.0	2.0	4,785	237.0

Table 2B - Estimated incidence, mortality and prevalence by cancer site for the year 2012 in Piedmont and Aosta Valley. 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	3,248	151.3	91.8	755	35.1	16.5	50,428	2,348.0
Stomach	379	17.7	7.8	262	12.2	5.1	1,853	86.3
Colon-rectum	2,052	95.6	42.0	734	34.2	13.6	14,828	690.5
Lung	893	41.6	19.6	684	31.9	14.3	1,964	91.5
Melanoma	627	29.2	20.4	55	2.6	1.3	7,648	356.4
Cervix	162	7.6	5.5	70	3.3	1.9	1,908*	89.2*

*Limited-duration prevalence at 15 years.

Table 3 - Comparison of crude rates (per 100,000) estimated by means of MI ratio and MIAMOD in the year 2012 in Piedmont

	Incidence		Mortality		Prevalence	
	MI ratio	MIAMOD	MI ratio	MIAMOD	MI ratio	MIAMOD
Men						
Prostate	209.5	219.6	33.5	34.9	1,506	1,741
Stomach	25.5	25.8	15.8	17.5	124	124
Colon-rectum	98.9	131.2	40.5	46.4	650	848
Lung	99.5	97.6	92.5	83.0	289	254
Women						
Breast	142.0	151.3	34.4	35.1	1,718	2,348
Stomach	16.3	17.7	10.2	12.2	81	86
Colon-rectum	79.4	95.6	33.0	34.2	626	691
Lung	38.2	41.6	29.1	31.9	113	92
Cervix	7.8	7.6	2.5	3.3	85	89*

MI, mortality-incidence. *Limited-duration prevalence at 15 years.

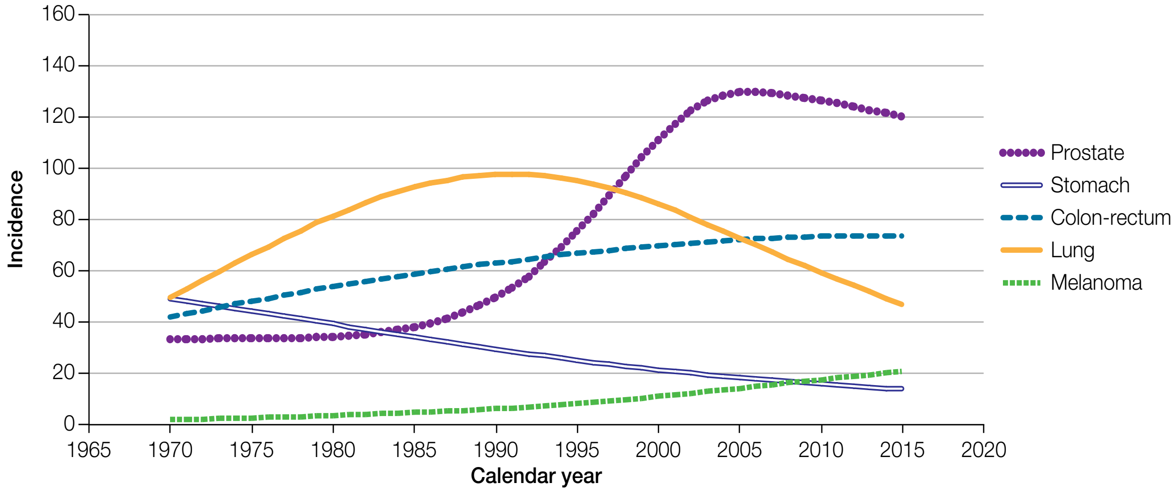


Figure 1 - Incidence estimates by cancer site in Piedmont and Aosta Valley in the period 1970-2015. Age-standardized rates (European population) per 100,000 person-years. Age 0-99 years, men.

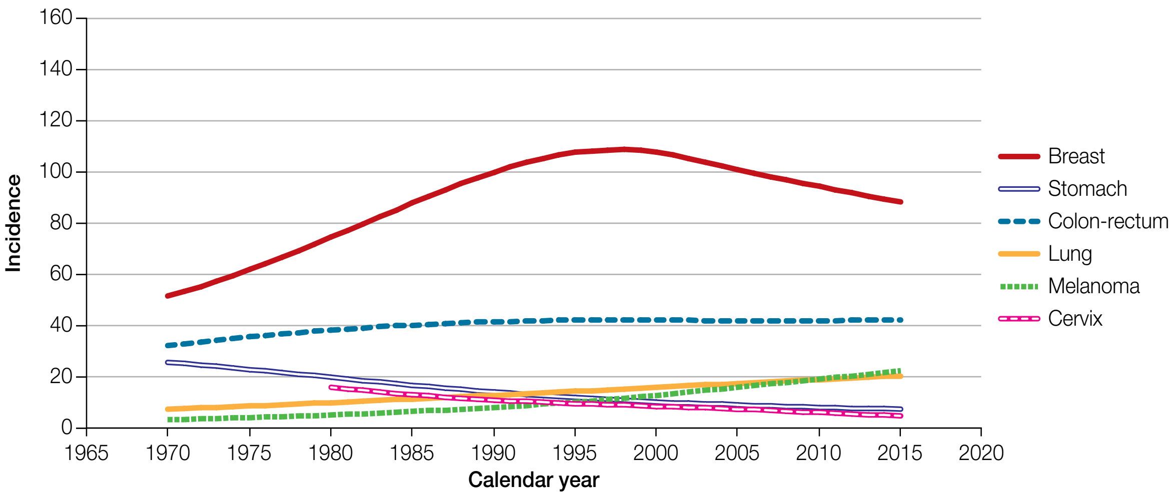


Figure 2 - Incidence estimates by cancer site in Piedmont and Aosta Valley in the period 1970-2015. Age-standardized rates (European population) per 100,000 person-years. Age 0-99 years, women.

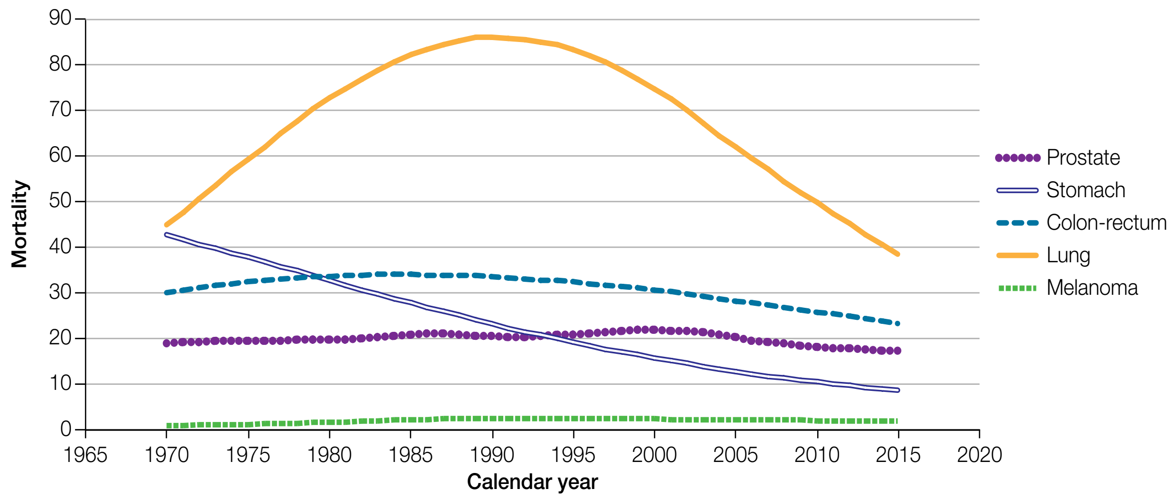


Figure 3 - Mortality estimates by cancer site in Piedmont and Aosta Valley in the period 1970-2015. Age-standardized rates (European population) per 100,000 person-years. Age 0-99 years, men.

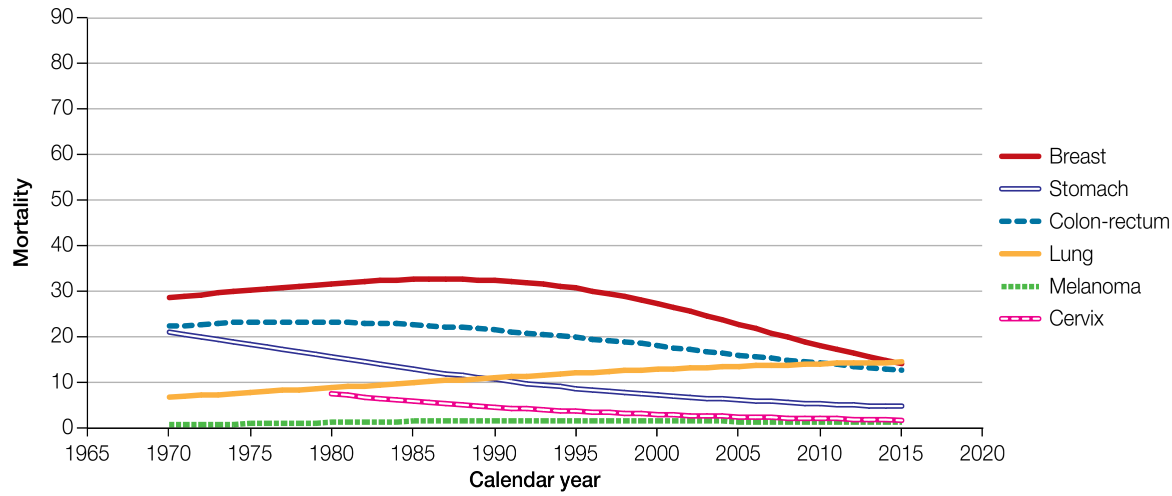


Figure 4 - Mortality estimates by cancer site in Piedmont and Aosta Valley in the period 1970-2015. Age-standardized rates (European population) per 100,000 person-years. Age 0-99 years, women.

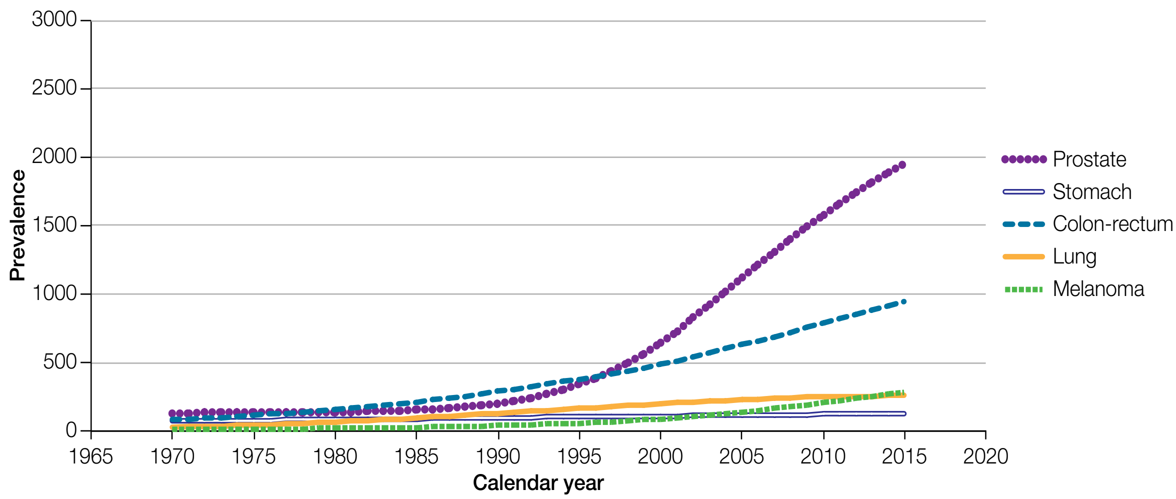
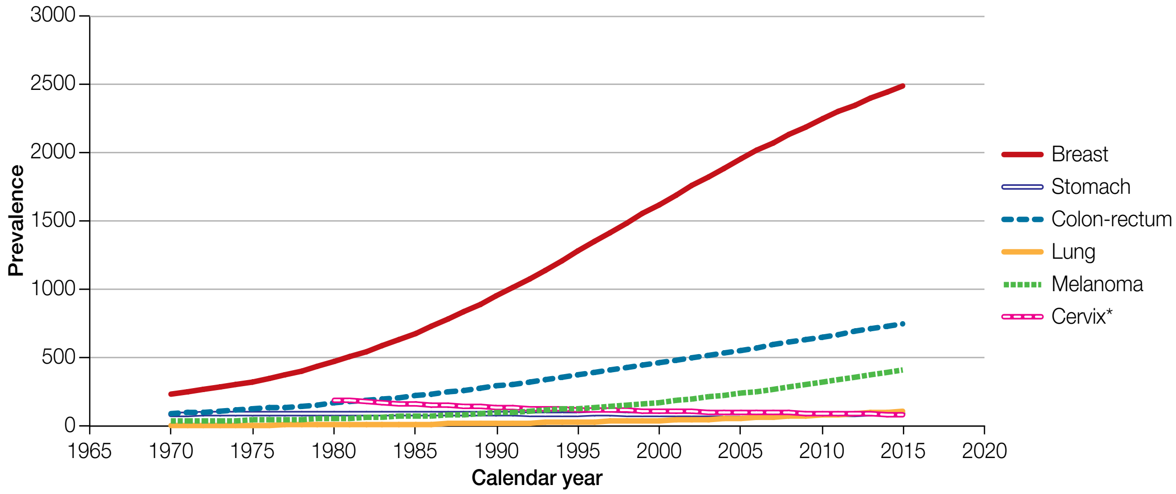


Figure 5 - Prevalence estimates by cancer site in Piedmont and Aosta Valley in the period 1970-2015. Crude proportion per 100,000 persons. Age 0-99 years, men.



*limited-duration prevalence at 15 years

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

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