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# Estimating regional cancer burden in countries with partial registration coverage: An application to all malignant neoplasms in Italy over the period 1970–2010

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## ABSTRACT

Regional epidemiological indicators of cancer burden are essential information for cancer surveillance and health resources planning, especially in countries with partial registration coverage and geographically variable risk patterns, such as Italy.

This paper presents a methodology to derive cancer incidence and prevalence at the regional and national scale and illustrates its application to all malignant neoplasms in Italy for the period 1970–2010.

The method, denoted as MIAMOD, is based on a back-calculation approach and derives cancer-specific morbidity measures by using official mortality data and model-based relative survival from local Cancer Registries data. The output includes time-trends and projections of a complete set of epidemiological indicators, i.e. mortality, incidence and prevalence.

Results for all cancers in Italy show different incidence patterns by gender and a pronounced regional variability among men: male incidence is estimated to decrease in almost all northern-central regions, while more stable or even rising trends are estimated in the southern regions. No incidence reduction is expected for women. Prevalence increases country-wide in both sexes.

The proposed approach can be applied to derive regional up-to-date time trends of cancer burden indicators in countries with local and sparse cancer registration systems. These estimates are useful for planning health services on a national and regional basis and for highlighting regional differences.

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## 1. Introduction

Continuous monitoring of the main cancer burden indicators is essential to evaluate progresses achieved and to define new programs of cancer control. The knowledge of these indica-

tors is relevant not only on the national, but also on the regional scale, as cancer levels and trends are often not geographically homogeneous within the countries and the appropriate local information for planning care policies and allocating resources is increasingly needed.

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In most of the European countries however, the only systematic data for the national and regional population regard mortality. The other indicators are provided by population-based Cancer Registries (CRs) covering only a fraction of the national population as, for instance, in France, Italy, Germany, Spain and Switzerland.<sup>1</sup>

Although population-based cancer statistics represent an invaluable and high quality source of information, they can only partially give a picture of the risk patterns and trends at the national and regional scale, when the population coverage is not statistically representative or even lacking. This is the case of Italy, where the population coverage of cancer registration varies from only 7% in southern regions to about 30% in the north and centre,<sup>2</sup> and where both cancer risk and survival vary highly from north to south.

Statistical models are therefore required to produce epidemiological indicators at national and regional scale and to project them in the near future, in order to assess cancer impact evolution and to quantify the health care demand, particularly in the regions not covered by CRs.

The aim of this paper is to present a methodology to derive cancer incidence and prevalence at the regional and national scale in countries with partial coverage of cancer registration and to illustrate an application of the method to all malignant cancers in Italy for the period 1970–2010.

The method, denoted as MIAMOD (mortality-incidence analysis model), is based on a back-calculation approach deriving cancer-specific morbidity measures starting from the knowledge of mortality and relative survival data<sup>3</sup> and has been already applied to derive national estimates in Italy.<sup>4</sup> The estimation procedure is substantially different from those based on the estimated mortality/incidence (M/I) ratio in CR areas used to produce national<sup>5,6</sup> or regional<sup>7</sup> incidence in other applications in European countries.

This approach has made it possible to estimate, for the first time, all cancers incidence and prevalence figures in all Italian regions.

## 2. Materials and methods

### 2.1. Data

Data needed for the analysis are obtained from two sources: the Italian National Institute of Statistics (ISTAT), with regard to mortality and population, and the EURO CARE-3 study<sup>8</sup> for cancer survival.

Mortality data for all malignant cancer sites except non-melanoma skin cancer (ICD IX rev.: 140–172, 174–208), and population data, by sex, age, calendar year and geographical region, both covering the period 1970–1999 have been included in the analysis.

In 1995 the coding system for mortality data changed from manual to automatic. This has produced a slight discontinuity in the cause-specific mortality time series. In particular for all malignant neoplasms, the automatic procedures turned out to attribute a lower number of deaths compared to manual coding. The appropriate correction coefficient (0.968) provided by ISTAT<sup>9</sup> has been applied to the 1970–1994 series in order to restore the continuity of mortality data.

Relative survival data for all malignant cancers in the diagnosis period 1978–1994 have been derived from the published results of the EURO CARE Project that compares cancer survival from population-based CRs across Europe.<sup>8,10,11</sup> The Italian registries included in the EURO CARE study, covering about 16% of the national population, refer to 13 areas: eight of them located in the North (Turin, Varese, Genoa, Veneto, Ferrara, Modena, Parma, Romagna), three in the Centre (Tuscany, Macerata and Latina) and only two (Ragusa and Sassari) representing the South (Table 1). The percentage of the regional population coverage is quite variable across the country, ranging from 6% (Ragusa) to 45% (Veneto and Emilia Romagna). The CRs with the longest time series are Varese, Parma (1978–1994) and Ragusa (1981–1994), while most of the others were established in the mid 1980s or later.

Cancer incidence data for the Italian CRs, used to validate the regional estimates, have been extracted from the EURO-CIM database.<sup>12</sup>

### 2.2. Estimation of regional and national cancer survival

The MIAMOD method requires as input regional or national estimates of cancer patients relative survival, which is the probability of dying from the specific cancer, excluding other competitive causes of death.

Relative survival (RS) for each region has been derived by modelling the grouped empirical data available from the EURO CARE-3 study, with parametric mixture cure models of the Weibull type.<sup>13,14</sup> In this class of models the population of patients is divided into a group of ‘cured’, with the same mortality as the general population, and a group of ‘fatal cases’ who will survive according to a Weibull distribution. Survival modelling enables one to extrapolate local survival rates, even in regions with no registration coverage, and to project them beyond the available registration period of 1978–1994.

A categorical covariate for the age at diagnosis (15–44, 45–54, 55–64, 65–74, 75+) and a continuous covariate for the period of diagnosis have been included in the survival models, so as to account for different age patterns and time improvements. The cumulative relative survival probability  $S_{x,i}(y,t)$  for the  $i$ th geographical area, age class  $x$ , year of diagnosis  $y$  and follow-up time  $t$  is therefore given by:

$$S_{x,i}(y,t) = \{P_{x,i} + (1 - P_{x,i}) \exp[-(\lambda_{x,i}t)^{\gamma_{x,i}}]\}^{\exp[\beta_i(y-\bar{y})]} \quad (1)$$

where  $P$  represents the proportion of cured cases,  $\lambda$  and  $\gamma$  are scale and shape Weibull's parameters and  $\beta$  is the log relative risk of being diagnosed 1 year later than an arbitrary reference year  $\bar{y}$  (equal to 1986, i.e. the central value in the period 1978–1994).

The parameters of this model were separately estimated for each sex and for five geographical areas. A regional area was used only when long-term local CR data were available: this is the case of Lombardia, Emilia-Romagna, and Sicilia. Two wider geographical areas, North-Centre and South, with homogeneous observed survival patterns, were considered to derive stable survival estimates in the regions with more recently established CRs or without any cancer registration system at all. The last column of Table 1 gives the survival estimation associated to each region.

**Table 1 – Regional distribution of the Italian Cancer Registries (CRs) included in the study, with the percentage of national and regional coverage and the reference period of survival data - the geographical area used for survival estimation in each region is given in the last column**

Regions	Cancer Registry	% of National population covered by CRs	% of Regional population covered by CRs	Period	Geographical area for survival estimation
<b>North</b>					
Piemonte	Turin	1.6	21.8	1985–1994	North-Centre <sup>a</sup>
Valle d' Aosta	–	–	–	–	North-Centre
Lombardia	Varese	1.4	9.0	1978–1994	Lombardia <sup>b</sup>
Liguria	Genoa	1.2	39.5	1986–1994	North-Centre
Trentino Alto Adige	–	–	–	–	North-Centre
Veneto	Veneto	3.5	45.1	1987–1994	North-Centre
Friuli Venezia Giulia	–	–	–	–	North-Centre
Emilia Romagna	Ferrara	0.6	9.1	1989–1994	Emilia Romagna <sup>c</sup>
	Modena	1.1	15.6	1988–1994	
	Parma	0.7	10.0	1978–1994	
	Romagna	0.7	10.9	1989–1994	
<b>Centre</b>					
Toscana	Tuscany	2.1	33.4	1985–1994	North-Centre
Umbria	–	–	–	–	North-Centre
Marche	Macerata	0.5	20.7	1991–1994	North-Centre
Lazio	Latina	0.9	9.4	1983–1994	North-Centre
<b>South</b>					
Abruzzo	–	–	–	–	South <sup>d</sup>
Molise	–	–	–	–	South
Campania	–	–	–	–	South
Puglia	–	–	–	–	South
Basilicata	–	–	–	–	South
Calabria	–	–	–	–	South
Sicilia	Ragusa	0.5	5.9	1981–1994	Sicilia <sup>e</sup>
Sardegna	Sassari	0.8	27.2	1992–1994	South

a CRs of Turin, Varese, Genoa, Veneto, Ferrara, Modena, Parma, Romagna, Tuscany, Macerata, Latina.  
b CR of Varese.  
c CRs of Ferrara, Modena, Parma, Romagna.  
d CRs of Latina, Ragusa, Sassari.  
e CR of Ragusa.

The national relative survival estimate has been obtained as the geometric weighted average of the northern-central and southern areas estimates, following a modelling approach described in a specific recent paper.<sup>15</sup> The proportions of expected all cancers incident cases in North-Centre and South were used as weights.

Two alternative time projection scenarios were evaluated to derive MIAMOD estimates: 1) a dynamic one, assuming survival rates increasing at the same rate of improvement estimated during 1978–1994 by  $\beta$  parameter; 2) a stationary one, assuming constant survival rates from 1994 onwards.

Except for national prevalence, all the estimates presented in this paper refer to the dynamic survival scenario.

### 2.3. Estimation of incidence and prevalence: the MIAMOD method

Incidence and prevalence estimates have been derived by the statistical method MIAMOD,<sup>3</sup> a back-calculation approach to estimate and project morbidity of chronic irreversible diseases, such as cancers, starting from mortality and survival data. An *ad hoc* developed software<sup>16,17</sup> has been used to produce these estimates. The method is based on the mathemat-

ical relationships relating mortality and prevalence, for a given cancer, to incidence and relative survival probabilities. For a birth cohort, the age-specific proportion of prevalent cases at age  $x$ ,  $P_x$ , is given by the following recursive formula:

$$P_x = \sum_{i=0}^{x-1} (1 - P_i) \mu_i S_{i,x} \quad (2)$$

where the term  $(1 - P_i)$  represents the probability to be free from cancer at age  $i$ ,  $\mu_i$  is the probability of being diagnosed with cancer between ages  $i$  and  $i + 1$ , and  $S_{i,x}$  is the relative survival probability up to age  $x$  for patients diagnosed at age  $i$ . With the assumption  $P_0 = 0$ ,  $P_x$  at each age  $x$  can be derived as a function of incidence and survival.

For the same birth cohort, the age specific probability to die ( $M_x$ ) for the given cancer is expressed as:

$$M_x = \sum_{i=0}^x (1 - P_i) \mu_i S_{i,x} d_{i,x} \quad (3)$$

the term  $d_{i,x}$  is the probability of dying from cancer at age  $x$  for patients diagnosed between ages  $i$  and  $i + 1$  who survive until age  $x$ .<sup>3</sup> Incidence probability is modelled in the logistic scale as a regular polynomial function of age ( $x$ ), period ( $t$ ) and cohort ( $c = t - x$ ) covariates:

$$\log it(\mu_{x,t}(\alpha)) = \alpha_0 + \sum_{i=1}^A \alpha_i(x)^i + \sum_{i=1}^P \alpha_{A+i}(t)^i + \sum_{i=1}^C \alpha_{A+P+i}(c)^i \quad (4)$$

To avoid collinearity problems, the linear period coefficient,  $\alpha_{A+1}$ , is excluded from Eq. (4) when polynomial degrees A, P, C are all different from 0. The set of incidence coefficients  $\alpha$  can be estimated by regressing the expected cancer-specific deaths derived from (3) and (2) on the observed deaths by calendar year and annual age. The regression coefficients are obtained through the maximum likelihood method, assuming a Poisson distribution for cancer deaths. The polynomial degrees and the parameters values  $\alpha$  are determined by fitting several nested models in a stepwise-like procedure. Once the incidence function has been estimated, prevalence is derived from Eq. (2).

Incidence is defined as the rate of new diagnoses observed in the disease-free population. Multiple tumours are therefore not included in the estimates.

Incidence is projected in the future by model (4), assuming that age and cohort coefficients do not change, while the period polynomial is substituted by its linear drift. Mortality and prevalence are consequently forward projected through Eqs. (2) and (3). The population is also projected by MIAMOD assuming that the number of newborns and the mortality rates for causes other than cancer will remain constant and equal to the last year of observation (1999).

All the estimates refer to the age class 0–84 years, as mortality data for the population older than 85 are too sparse to be modelled. Only with the purpose of comparing the estimates with other published data, incidence for ages 85+ was

extrapolated from incidence-mortality ratio in the 80–84 age group.

The age-adjusted rates are based on the standard European population.

### 3. Results

#### 3.1. Incidence APC models

For each region, as well as for Italy, an independent incidence model's estimation was carried out by using a different combination of age, period and cohort covariates. Table 2 reports the APC models chosen for each geographical area. The corresponding coefficient of determination  $R^2$  is also given to evaluate the fit to cancer mortality data. Full APC models, with a period polynomial not exceeding the degree 2, were used for men in almost all the regions and for women in northern and central Italy. Age and cohorts effects adequately described cancer trends for women in all the southern regions, where the decline of cancer mortality is less pronounced. The models' goodness of fit was very high for Italy ( $R^2 = 0.999$  for men and 0.998 for women) and for all the regions ( $R^2 > 0.870$ ), even for the less populated ones, such as Molise and Valle d'Aosta, where the statistical variability of mortality data was relevant.

#### 3.2. Validation of MIAMOD estimates

The regional estimates were compared to the corresponding incidence and mortality rates observed in the areas covered

**Table 2 – Age (A), period (P) and cohort (C) polynomial models used to derive regional and national estimates of incidence and prevalence in Italy - the coefficient of determination  $R^2$  is reported for each model**

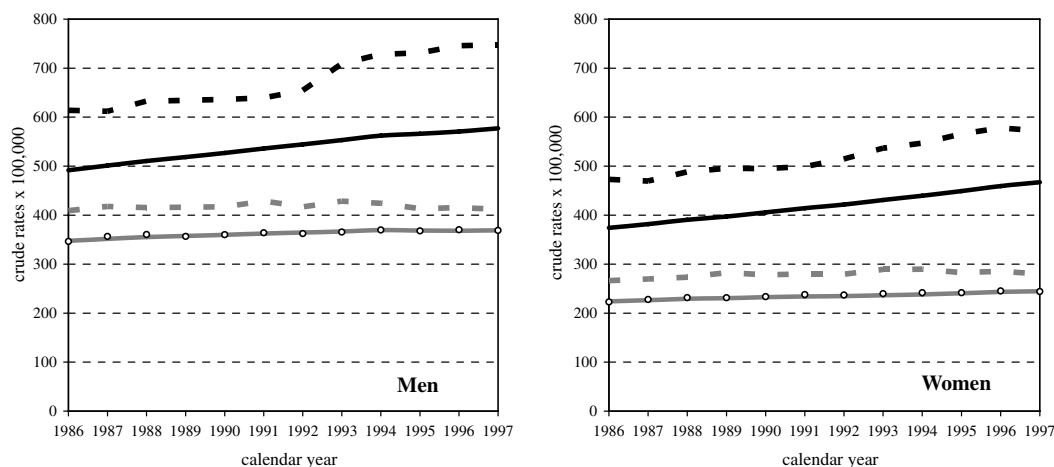
Regions	Men				Women			
	Polynomial order			$R^2$	Polynomial order			$R^2$
	A	P	C		A	P	C	
<b>North</b>								
Piemonte	5	2	3	0.997	5	2	3	0.995
Valle d'Aosta	3	2	2	0.926	4	0	2	0.870
Lombardia	5	2	2	0.997	5	2	4	0.996
Liguria	4	2	2	0.994	4	2	3	0.992
Trentino Alto Adige	3	2	2	0.982	4	0	3	0.986
Veneto	4	2	2	0.992	5	2	3	0.993
Friuli Venezia Giulia	4	2	2	0.993	4	2	3	0.991
Emilia Romagna	5	2	3	0.996	4	2	4	0.994
<b>Centre</b>								
Toscana	5	2	2	0.996	4	2	3	0.994
Umbria	3	2	2	0.986	4	2	3	0.984
Marche	4	2	2	0.993	4	2	2	0.990
Lazio	4	2	3	0.996	4	2	2	0.992
<b>South</b>								
Abruzzo	4	2	2	0.992	4	0	2	0.981
Molise	3	0	2	0.961	4	0	2	0.935
Campania	5	0	2	0.996	5	0	2	0.990
Puglia	4	2	3	0.995	5	0	2	0.989
Basilicata	3	0	2	0.976	5	0	2	0.959
Calabria	4	2	2	0.991	4	0	2	0.981
Sicilia	4	2	2	0.996	5	0	2	0.993
Sardegna	3	2	3	0.990	4	0	2	0.980
<b>ITALY</b>	5	2	4	0.999	7	2	3	0.998

by cancer registration. Full and direct comparisons were not possible in principle, since the large majority of Italian CRs do not cover the entire regional population; CR statistics include multiple tumours and cover a shorter time-period. Despite these limits the validation of the regional estimates against the local data, too space-consuming to be reported here, showed a general consistency both in levels and in time trends. An overall validation of MIAMOD estimates is given in Fig. 1 where national incidence and mortality estimates for all cancers and ages 15+ are compared against the time trends for the pool of Italian Registries, recently published by AIRT.<sup>18</sup> The AIRT pool includes only the nine registries (Torino, Varese, Genova, Veneto, Modena, Romagna, Parma, Firenze-Prato, Ragusa) covering the common registration period 1986–1997. The mortality rates observed in the CR covered population are higher by 14% in men and 16% in women than the national rates, since CRs are concentrated in the higher-risk North-Centre regions. Correspondingly, observed incidence is higher by 20% in men and 19% in women than the estimated national incidence, which does not include multiple

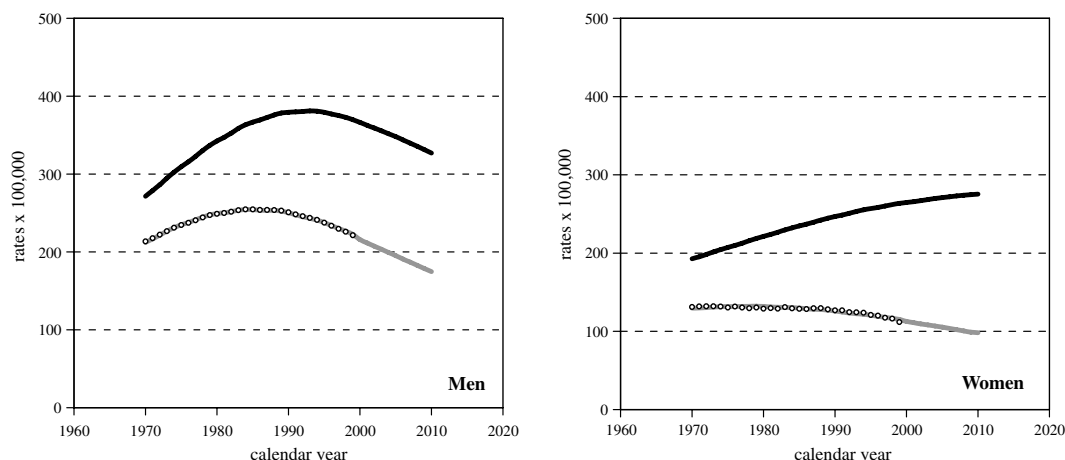
tumours. Time trends are very similar. As a further check, by aggregating all regional estimates we obtained the same results as the independent national estimate, with average differences smaller than 1%.

### 3.3. National and regional time trends

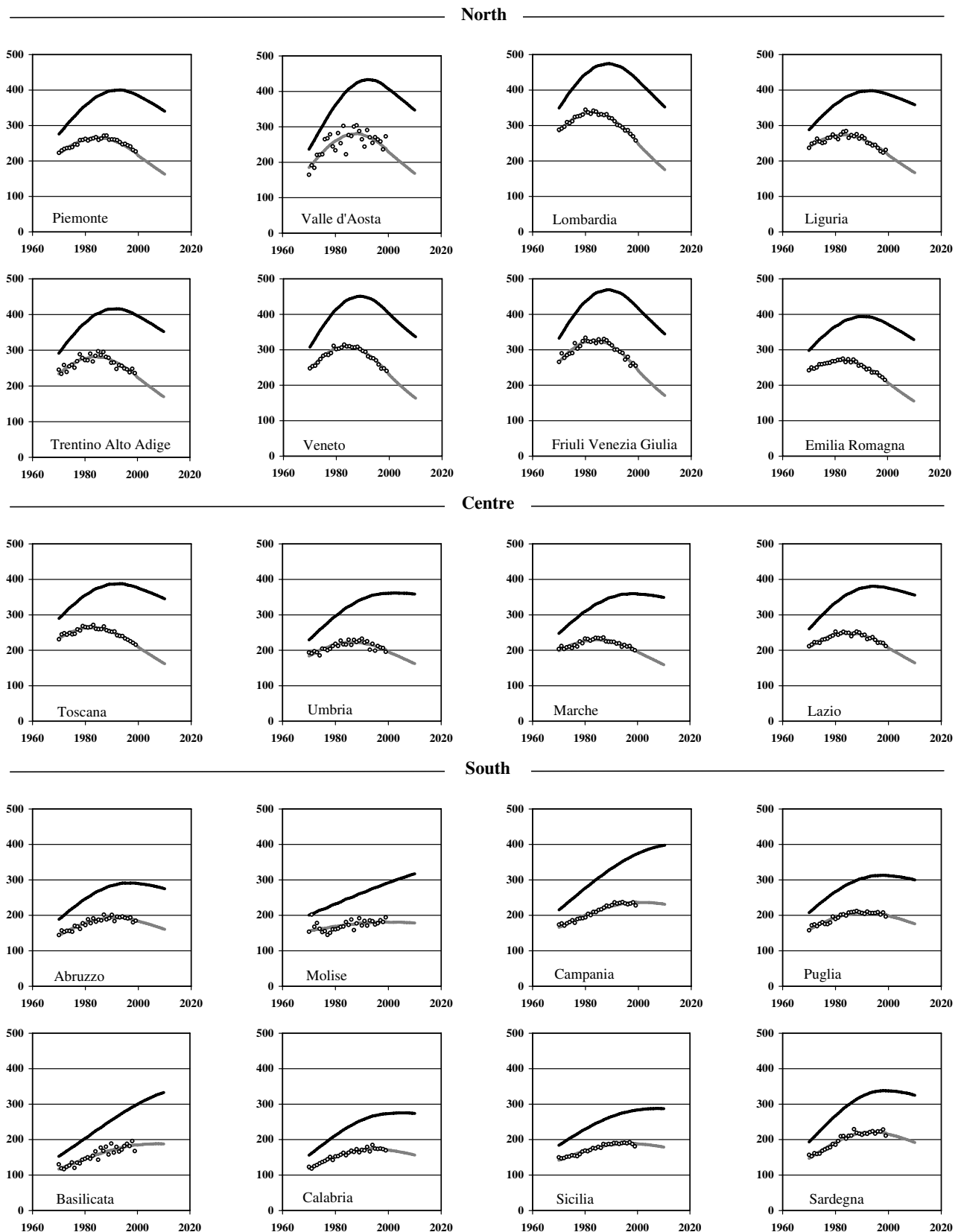
Age-adjusted rates for all cancers incidence and mortality in Italy from 1970 to 2010 are shown in Fig. 2. Male mortality and incidence were steeply rising from 1970 onwards, reached their peak values in 1985 and 1995 respectively (250 and 380 per 100,000), declined thereafter and are estimated to continue dropping even in the projection period (175 and 325 per 100,000 in 2010). The pattern is quite different for females, as no reduction is expected for incidence, varying from 198 in 1970 to 280 per 100,000 in 2010, while cancer mortality slightly, but constantly, decreased from 1985 onwards including projections (about 100 per 100,000 in 2010). The estimated lifetime risk of developing cancer up to 74 years of age starts to decrease, only in men, for the cohorts born after 1940.



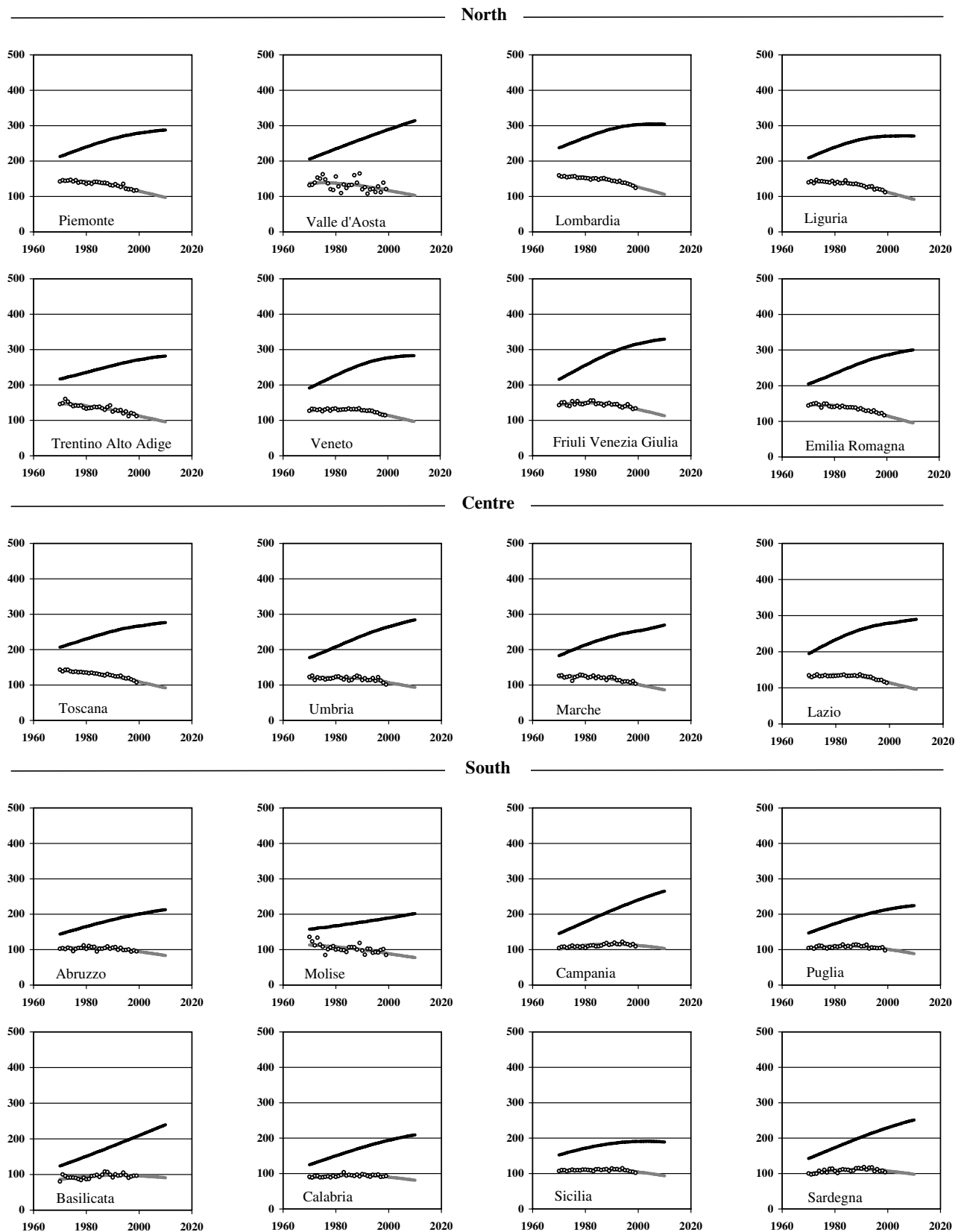
**Fig. 1** – Crude mortality and incidence rates of all cancers estimates in Italy (grey and black continuous lines) compared to Italian CRs pooled data (dashed lines) and observed national mortality rates (dots) in the period 1986–1997. Data and estimates refer to ages 15+.



**Fig. 2** – Mortality and incidence estimates 1970–2010 for all cancers in Italy (grey and black continuous lines) compared to observed mortality (dots). Age standardised rates (European population) per 100,000, age 0–84 years.



**Fig. 3 – Regional mortality and incidence estimates 1970–2010 (grey and black continuous lines) for all cancers in Italian men compared to observed mortality (dots). Age standardised rates (European population) per 100,000, age 0–84 years.**



**Fig. 4 – Regional mortality and incidence estimates 1970–2010 (grey and black continuous lines) for all cancers in Italian women compared to observed mortality (dots). Age standardised rates (European population) per 100,000, age 0–84 years.**



These national patterns mainly reflect time trends of northern-central regions that clearly differ from those in the south (Figs. 3 and 4).

A strong reduction of mortality in northern-central regions started approximately from the mid 1980s in men (Fig. 3); in southern regions, instead, mortality is estimated to level off or to slightly decrease only after the 1990s. An equally strong reversal was estimated from the 1990s for incidence rates in almost all regions (except Umbria and Marche), leading to significant reductions in 2010, with levels ranging from 350 to 380 per 100,000. On the contrary, in the South, incidence increased over the period 1970–1999 and is expected to remain either stable or increasing (Molise, Campania and Basilicata) in projections.

The decline of cancer mortality among women observed in Italy since 1985 is the result of a pronounced decrease limited to northern and central regions (Fig. 4). In southern regions, mortality rates instead were stable or even weakly increasing until 1999 and are expected to decline only in the projection period. Increasing trends throughout the entire study period characterise female cancer incidence in all areas. Only in some regions (especially Lombardia, Liguria, Veneto and Sicilia) is incidence estimated to level off during the projection period.

### 3.4. Cancer prevalence in the years 1999 and 2010

Regional and national prevalence proportions in 1999 and in 2010, i.e. at the end of the projection period, are given in Table 3.

In 1999 the estimated proportion of persons of age 0–84 living in Italy with a past cancer diagnosis was 2.1% for men and 2.6% for women. Prevalence rates for men and women are significantly higher in northern (2581 and 3202 per 100,000) and central (2331 and 2917) areas than in the South (1408 and 1642). This result is consistent with the North-to-South gradient in incidence risks and survival levels. As a consequence of incidence, survival and age structure dynamics, the proportion of prevalent cases is predicted to rise up between 1999 and 2010, in both sexes. The rise of prevalence proportion is expected to be +3.7, 4.0 and 3.4% per year, in northern, central and southern areas, respectively, among men, while about +3.5% in all the geographical areas among women. The annual percentage change (APC) estimated for the national population, assuming survival increasing after 1994, is about +3.5% in both sexes; under the assumption of stable survival rates, the annual growth in the prevalence proportions is less marked both for men (+1.6%) and women (+2.3%).

## 4. Discussion

The MIAMOD method was used for estimating cancer incidence and prevalence, starting from official mortality data and survival estimates by region. The latter are obtained through an appropriate modelling of population-based local data.

The main strengths of the method are: i) the wide set of cancer burden indicators, including incidence, prevalence and mortality provided for each geographical area; ii) time-

**Table 3 – Regional estimates of all cancers prevalence in Italy for the years 1999 and 2010 with the Annual Percentage Change (APC) - projections according to dynamic and stationary survival scenarios are reported for Italy - crude proportions per 100,000, age 0–84 years**

Region	Men			Women		
	1999	2010	APC	1999	2010	APC
<b>North</b>	<b>2581</b>	<b>3852</b>	<b>3.7</b>	<b>3202</b>	<b>4654</b>	<b>3.5</b>
Piemonte	2587	4023	4.1	3202	4653	3.5
Valle d'Aosta	2624	4015	3.9	3098	4624	3.7
Lombardia	2516	3760	3.7	3319	4764	3.3
Liguria	2917	4313	3.6	3565	4970	3.1
Trentino A.A.	2147	3222	3.8	2622	3738	3.3
Veneto	2451	3422	3.1	2847	4189	3.6
Friuli V.G.	2913	4119	3.2	3656	5325	3.5
E. Romagna	2709	3920	3.4	3188	4823	3.8
<b>Centre</b>	<b>2331</b>	<b>3591</b>	<b>4.0</b>	<b>2917</b>	<b>4300</b>	<b>3.6</b>
Toscana	2614	3873	3.6	3123	4510	3.4
Umbria	2422	3752	4.1	2951	4412	3.7
Marche	2352	3623	4.0	2807	4078	3.5
Lazio	2122	3357	4.3	2806	4202	3.7
<b>South</b>	<b>1408</b>	<b>2031</b>	<b>3.4</b>	<b>1642</b>	<b>2419</b>	<b>3.6</b>
Abruzzo	1626	2231	2.9	1829	2674	3.5
Molise	1605	2382	3.7	1797	2569	3.3
Campania	1469	2195	3.7	1687	2589	4.0
Puglia	1411	2002	3.2	1664	2502	3.8
Basilicata	1408	2199	4.1	1645	2628	4.4
Calabria	1271	1862	3.5	1522	2276	3.7
Sicilia	1269	1737	2.9	1536	1993	2.4
Sardegna	1573	2357	3.7	1734	2814	4.5
<b>ITALY dynamic surv.scen.</b>	<b>2105</b>	<b>3120</b>	<b>3.6</b>	<b>2580</b>	<b>3750</b>	<b>3.5</b>
stationary surv.scen.	–	2496	1.6	–	3323	2.3



trends with long-term projections derived for each indicator; iii) the flexible estimation procedure, based on the modellisation of cancer survival which allows one to incorporate the survival time trends and to control the assumptions on survival time-projections. On the other hand, the method depends on the quality of mortality data (which for all cancers combined can be considered high) and of survival data. Furthermore, particular care in modelling survival data is required to obtain reliable estimates of cancer incidence and prevalence. A potential limit of the method is that it includes only the first occurrence of a specific tumour. The consequent underestimation is negligible when dealing with a single cancer site, but can be around 5–10% for all malignancies.

No survival data modelling is instead required for the M/I ratio method<sup>5</sup> so that it is widely applied to derive point estimates of incidence and, in combination with CR survival data, partial prevalence at 5 years from diagnosis.<sup>19</sup> An upgrade of the M/I method, using model-based trends of the M/I ratio to reproduce potential improvements of patients' survival and allowing short-term projections, has been proposed and applied in France.<sup>7,20</sup> An alternative approach to complete prevalence estimation is the one introduced by Colonna et al.<sup>21</sup> that relies on incidence and mortality data.

The application to all malignant neoplasms in Italy provides three main epidemiological results: the different cancer incidence patterns observed for men and women; the decrease of male age-standardised incidence in almost all northern-central regions; the progressive increase of prevalence.

Differences between men and women are mainly attributable to the gender-specific case-mix of sites in all cancers, and trends are supposed to be largely driven by the major cancer sites: the downward trends observed for Italian men are explained by the decline of lung and stomach cancer incidence and mortality,<sup>18,22,23</sup> among women, the decreasing trends of stomach cancer are compensated by the parallel increase of lung cancer diagnoses, thus incidence and mortality patterns mostly reflect breast and colorectal cancer trends.<sup>23,24</sup> The marked regional variability of cancer incidence in men reflects the high variations of levels observed among the Italian CRs for prostate cancer, which has recently become the leading tumour site in the male population.<sup>25</sup> The regional variability is, instead, less pronounced among women, due to the lower geographical variations of breast cancer incidence levels and trends.

The incidence reduction estimated for men in northern-central regions from 1995 is the direct consequence of i) the mortality decline observed since the end of the 1980s, and ii) having assumed in survival projection the same rate of improvement as that observed in 1978–1994 (about 3% per year). Due to the contemporary rise of incidence in the southern regions, the North-to-South gap in the next future is predicted to become smaller than in past decades.

Three separate factors contributed to the increase of prevalence proportions for both men and women in the study-period: the progressive population ageing, the improvements in cancer survival and the incidence dynamics. Prevalence projections in 2010 according to stationary/dynamic survival time-trend differ by 13% for women and 25% for men (Table 3). This is largely a consequence of the marked rise of prostate cancer survival after the PSA test introduction, producing a

higher rate of improvement in men than in women. Thus, in spite of the important changes being under way, cancer burden in Italy is expected to represent a still increasing problem in health care planning in the future.

These results, and in particular, projections for the period 2000–2010 depend on the assumptions made to derive survival estimates for the study-period. Cancer survival has been modelled by assuming: i) different patterns between northern-central and southern areas, and ii) survival levels increasing after 1994 at the same rate as during 1978–1994. The first assumption turned out to give the best model adaptation to the empirical EUROCARE data. The second one seemed the most reasonable in absence of data after 1994, since it was supported by the incidence reduction observed for lung cancer in men and for stomach cancer in both sexes, by the stabilisation of incidence for colorectal and breast cancer in women and by the recent increase in cancer screening coverage in Italy.<sup>18</sup> Furthermore, more up-to-date studies of cancer survival trends in US, Europe and even Italy<sup>26–30</sup> confirmed the continuous increase of survival after 2000 for colorectal cancer, breast and prostate.

The recently published regional estimates of cancer incidence in Italy for the year 2001<sup>31</sup> derived by applying the M/I ratio method,<sup>5</sup> were systematically higher than those presented in this paper. The difference is mostly attributable to the inclusion of multiple tumours and age-classes over 85, but also to the different method. In particular, the M/I ratios were obtained by modelling CR mortality and incidence data for the period 1993–1998, and then applied to the regional cancer mortality data for the year 1998. Finally, the estimated incidence rates were applied to regional populations in 2001, thus assuming no survival improvement during 1998–2001.

The estimation method proposed can be applied in countries with partial registration coverage to derive up-to-date time trends of cancer incidence and prevalence both at national and regional scale. The population-based picture of the main epidemiological indicators by calendar year, age and region is crucial information for planning health care services on a regional basis and to evaluate the present regional differences and their future tendencies. For instance, the results for Italy show that the undeniable progresses against cancer achieved at national level, especially in the male population, seem to be spread with a certain delay to the southern regions.

The application to all malignant cancers is part of a wider project aimed at producing and disseminating systematic regional estimates of cancer burden for the main neoplasms in Italy.

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## Conflict of interest statement

None declared.

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