Incidence and prevalence of all cancerous diseases in Italy:
trends and implications

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Abstract

The burden of cancer in ageing populations is causing great concern, particularly in Italy with Europe's fastest growing elderly population. Studying all cancers combined in one group, although of limited medical value, is of great interest from the viewpoints of public health, epidemiology and the economy. Using mortality data and an estimate of cancer patients' survival we have estimated and projected incidence and prevalence in Italy of all cancers combined in one group. Five major phenomena are highlighted in the paper: (1) the decrease in the age-adjusted cancer mortality rates among females and the stable mortality rates among males since 1990; (2) the changing pattern of cancer incidence since 1990, it has started to decrease for females and is stabilising for males; (3) the decrease in cancer incidence among males and females born after 1940; (4) the increase in the proportion of cancer patients that are cured with calendar years of diagnosis; (5) the increase in the total and the healthy life expectancy (i.e. cancer-free) among the Italian population since 1970. The declining and flat trends in age-adjusted cancer incidence and mortality rates since 1990 is the combined effect of survival improvements and cancer risk reduction for younger cohort groups, after 1940. These favourable trends contribute to the increase in healthy life expectation, thus supporting the idea that we live longer and healthier. © 2001 Elsevier Science Ltd. All rights reserved.

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1. Introduction

Cancer is a major concern all over the world causing deprivation of quality of life and premature mortality and demanding the allocation of large amounts of resources to provide diagnostic and care facilities. The study and estimation of the cancer epidemic as a whole, with respect to its dimension, trends and projections, is essential for planning health services, allocating resources, administering medical care facilities, assessing the relative burden of cancer with respect to mortality and deprivation of quality of life, and evaluating the economic impact of cancer. Furthermore, in ageing populations, as in Europe and in particular Italy where a rapid increase is being observed in the size of its elderly population, the cancer burden is expected to be a major problem, and the study of all cancers combined is therefore of great relevance to public health.

Mortality data, available in Italy since 1970, have been used to describe the behaviour of cancer with respect to time and occurrence in different geographical areas [1]. However, improvements in cancer patients' survival, with the possibility of cure for some forms of cancer, has led the incidence and mortality rates to diverge. Mortality alone is not able to provide detailed estimates of cancer burden and, for cancers with good prognosis, is not a suitable basis to study associations between risk factor changes and cancer occurrence.

In Italy, incidence and survival information have recently become available from local population-based cancer registries that cover approximately 10% of the Italian population. The ITACARE study [2], a collaborative action aimed at studying the variability of cancer patients' survival in Italy and involving 11 Italian cancer registries, for the first time provided weighted estimates of relative survival from all cancers combined.
to represent the Italian population as a whole. The availability of mortality data and cancer patients’ survival, allow cancer incidence and prevalence to be estimated for the entire Italian population, by using appropriate methods.

The aim of the study was to present up-to-date estimates of cancer incidence and prevalence in Italy and projections through to 2000, of all cancers combined in one group, based on a statistical method that uses mortality data and the recently available information on cancer patients’ survival. Mortality, incidence, prevalence and patients’ survival time trends will be presented and discussed, along with the impact of cancer disease on the total and healthy life expectancy in Italy.

2. Patients and methods

2.1. Mortality data

Official population and all causes mortality, including mortality from all malignant neoplasms (ICD9 140-208, excluding 173), by single age and calendar years were obtained from the Italian National Bureau of Statistics (ISTAT) [3], for the years 1970 to 1993.

2.2. Patients’ survival

Relative survival rates of all malignant neoplasms combined were obtained at the national level, from the ITACARE study [2,4]. In this study, the relative survival rates were estimated from survival data of patients registered between 1978 and 1989 by nine out of the 11 Italian cancer registries that provided data for all cancer sites. The analysis included only primary tumours and excluded death certificate only cases and those discovered at autopsy. By weighting age- and time-specific cancer registry (CR) survival estimates we derived a national estimate. The weights used were the age- and period-specific incidence cases expected for each Italian region, on the basis of incidence observed by the registries belonging to that region or even neighbouring regions. Although this estimate cannot be seen as strictly representative of the whole Italian population, it is a reasonable estimate of it. Weighted Italian relative survival curves are plotted in Fig. 1 by gender and period of diagnosis, 1978–1981 and 1986–1989. Females show better survival for all cancers combined than males. During the period 1978–1989, 5-year survival showed an important improvement, nearly 17% for females (27% for males).

A mixture survival model [5,6] was fitted to age- and period-specific estimated weighted relative survival rates, in order to extrapolate the survival beyond the observed 10 years of follow-up. It is assumed that a proportion $P$ of patients to be cured for cancer will experience the same mortality risk as the general population of a similar age. The remaining fraction $1 - P$ represents the proportion of fatal cases, i.e. patients that will eventually die from cancer. The relative survival of fatal cases is assumed to be Weibull distributed, while for cured cases it is 1, since they do not die of cancer. The relative survival function of the whole population of patients is obtained as a mixture of the corresponding survivals:

$$S(t) = P + (1 - P)\exp[-(\lambda t)^\beta].$$

The mean survival time of fatal cases is given by $\lambda^{-1}\Gamma(1 + \beta^{-1})$, where $\Gamma$ is the gamma function.

In order to back-calculate incidence and prevalence from mortality data, survival is needed for the years before 1978. We have assumed that survival figures for the years before 1978 are at the same level as in 1978.

2.3. The back-calculation model: MIAMOD

Incidence and prevalence are estimated from mortality and survival by a method (MIAMOD) that has been extensively described [7,8] and applied in previous works [9–12]. The fundamental elements of the model are as follows.

We assume the disease incidence hazard, $I$, to be a continuous function of age $x$, time $t$, and a set of parameters $\beta$ (to be estimated). A polynomial function of age, year (period), and year of birth (cohort) in the logistic scale is considered as a rather general and flexible way to describe different patterns of risk:

$$\logit \mu(x, t) = \beta_0 + \sum_{i=1}^{a} \beta_i \text{(age)}^i + \sum_{j=1}^{b} \beta_j \text{(year)}^j + \sum_{k=1}^{c} \beta_k \text{(cohort)}^k.$$
The set of parameters $\beta$ completely determines the incidence function $\mu$ and therefore the incidence rates at each age $x$ and time $t$. From the mathematical relationships holding among incidence, prevalence, survival and mortality for the birth cohort, when the disease under consideration is assumed to be irreversible [7], it is possible to express the expected cause-specific mortality as a function of incidence, given by Eq. (2) and, therefore, as a function of the unknown parameters $\beta$, say $M(x, t; \beta)$.

The method consists then in fitting the expected mortality $M$ to the observed mortality, in order to estimate the coefficients of the incidence function. The order of the polynomials and the coefficients are the parameters to be estimated. This is done by the maximum likelihood method and the order of the age, period and cohort polynomials is found by fitting several models in a stepwise-like procedure. Asymptotic standard errors of the maximum likelihood estimates of the parameters are computed as the inverse of second derivatives of the log-likelihood function matrix [8]. Standard errors of incidence and prevalence estimates are then derived.

As in any age, period and cohort model, a certain amount of extrapolation is implied, and estimates are derived combining information from different birth cohorts on age and period. Consider the case of an age and cohort model, with no period. In this case, there is a unique age profile that applies to any birth cohort as completely determines the cancer incidence at age $x$. Standard errors of the cumulative risk are derived from the covariance matrix of the estimated polynomial coefficients by using the delta method [13].

Projections of incidence rates for the period 1994–2000 were calculated on the basis of the incidence function obtained for the period 1970–1993. For this purpose, age and cohort estimated effects were assumed to persist also during the projection period and projected survival rates. Two types of projections will be presented: (i) conservative, i.e. with survival rates that are assumed to be the same as the ones estimated in the period 1986–1989, (ii) optimistic, i.e. with survival rates continuing to increase at the same rate as estimated during 1978–1989.

Mortality and morbidity/mortality life tables are calculated [8] in order to compute total life and cancer-free life expectancy. Both life tables are cross-sectional representing the combined experiences of mortality and morbidity of a population in a particular year. Mortality life tables are constructed using either the observed or projected general mortality rates. In morbidity/mortality (double decrement) life table [14], either cancer occurrence or death from any other cause removes individuals from the healthy population. Differences in the life expectancy between mortality and morbidity/mortality life tables provide information on the average number of years expected for the population to be spent as a cancer patient, i.e. life expectancy associated with cancer.

3. Results

Fig. 2 reports trends of mortality from all malignancies in Italy, 1970–1993, along with expected mortality from the MIAMOD application. Crude cancer mortality is shown as increasing in Italy. The increasing trend is faster for males, although the increase appears to be slowing down in recent years, for both males and females. Population ageing is the major factor for this increase. Age-standardised rates (ASRs) show mortality for males to increase and then stabilise at 23 per 10,000 population, and for females to reduce slightly from 15 to 14 per 10,000 population, from 1970 to 1990.

Table 1 reports results from modelling relative survival with the mixture model [1]. The proportion cured among young patients (<55 years) is approximately 34% for males and approximately 49% for females; this proportion declines with age. For the mean survival time, for uncured patients, only a moderate shortening with age was estimated. For males, the improvement in survival in more recent years is due to an increase in

![Fig. 2. Observed (diamond) and estimated (continuous line) crude all cancers mortality by sex, Italy 1970–1993. Rates x 10,000.](Image 321x86 to 534x233)
both the proportion cured and the mean survival time of the fatal cases. For females, the improvement is due to an increase in the proportion cured only.

Cancer incidence and prevalence for Italian males and females were obtained by the MIAMOD method applied to the mortality data and patients’ survival estimates. After a backward stepwise procedure the final age, period and cohort model contained only age and cohort effects (7th order polynomial in age and 4th in cohort for males, 8th and 3rd, respectively, for females).

The estimated number of incident cancers increased more for males than for females (Fig. 3). Although the number of incident cancers in males is larger than in females the prevalence is higher amongst the females, mostly due to the better survival from cancer in females. Yearly incidence among females in recent years is estimated to be nearly constant while for males it is still increasing. As a consequence, the increase in prevalence over time is slowing down for females, while it is continuing to increase for males. Overall, 138,000 cancer deaths, and 239,000 new cases of cancer are estimated to occur in Italy in the year 2000, leading to 1,306,000 prevalent cancer cases. The expected cancer prevalence increase in the year 2000 is over 70% with respect to 1970, and 23% with respect to 1990, approximately 80% of which is due to the ageing of the population.

Table 2 presents for years 1970, 1980 and 1990 the age-specific observed mortality and estimated incidence and prevalence rates. The respective projections are given for the year 2000, according to the conservative hypothesis on the future survival trend. For both males and females, the 0–84 year old crude mortality and incidence rates increase systematically from 1970 to 2000. Age-adjusted (using the 1970 Italian population as standard) mortality, incidence and prevalence rates increased by 15, 20 and 25% for males from 1970 to 1990, respectively. For females, mortality decreased by 6%, while incidence and prevalence increased by 8 and 10%, respectively, in the same period. However, in the period 1990–2000, incidence and mortality rates will stop increasing for males, while for females incidence rates will start to decrease.

The analysis of the age-specific rates in the period 1970 to 1990 shows that mortality, incidence and prevalence rates are slightly decreasing in the younger age groups, while still increasing in the older age groups. For males less than 45 years and females less than 55 years of age, mortality and incidence are decreasing from 1970 to 2000. From 1980, mortality and incidence are decreasing for males less than 55 years and females less than 65 years. The same occurs from 1990 for males under 65 years and females under 75 years, respectively. Prevalence, as cumulative incidence, has a slight delay in showing changing trends compared with incidence and mortality. The changing cohorts involved are the 1930–1934 birth cohorts for males and 1920–1924 birth cohorts for females. This reflects a cohort effect in which the risk of cancer is reducing for the younger birth cohorts after 1920–1930.
Fig. 4 reports cumulative risk of cancer by birth cohort, up to 74 years of age, along with standard errors of the estimates. The increase and subsequent decrease in the rates is more significant for males (approximately a 75% increase) than for females (19%). Estimation of birth cohort effects necessarily involve incidence projections made by the age, period and cohort model [8], since no one complete cohort was actually observed between 1970 and 1993.

Table 3 reports several indicators of life expectancy for the Italian population, in different calendar periods, that can be used to evaluate the demographic impact that cancer can have on a population: total, cancer-free, years expected to be lived with cancer, with cancer eliminated as cause of death. Life expectancy refers to a hypothetical cohort experiencing the cross-sectional observed/estimated mortality in a calendar year, e.g. 1970, 1990 and 2000 in Table 3. The Italian life expectancy at birth increased by 4.8 and 5.7 years for males and females, respectively, in 1990 with respect to 1970; females experiencing an increase of almost 1 year more than males. In addition, cancer-free life expectancy increased, although to a lesser degree. This means that most of the years of life gained during the last two or three decades of this century are of healthy ones with respect to cancer, i.e. cancer-free. The years expected to

![Graph of Fig. 4](image-url)
live with cancer were higher for the female population as the result of the better prognosis for female cancers. Years lived with cancer moderately increased for the Italian population by half a year between 1970 and 1990, representing only 10.4 and 8.8%, of the total lifetime gained for males and females, respectively. Eliminating cancer as a cause of death, life expectancy at birth would increase more markedly for males than for females and both sexes would experience the same increase in life expectancy of 6.2 years between 1970 and 1990.

### 4. Discussion

Quality of mortality data for some specific cancer sites can be questionable due to misclassification among related or neighbouring sites, such as the colon and rectum or cervix and corpus uterus cancers. In contrast, mortalities from all cancerous diseases can be affected only by possible misclassification with other non-cancer causes. However, in Italy this is known to occur only rarely.

Cancer patients’ survival in Italy was estimated as the weighted mean of nine Italian cancer registry estimates. With weights based on the expected number of new cancer cases by region, we obtained a survival estimate attributable nationwide in Italy, although the cancer registries’ distribution is not uniform to the country area. The mixture survival model, used to extend available survival estimates to the long term, was very efficient in fitting well the age- and period-specific survival rates. Modeled age- and period-dependent survival rates were considered in the estimation process. For the incidence and prevalence estimation process, we needed relative survival data for an extended period before the observation period. We assumed the relative survival for all cancers combined remained stable at the 1978 level, for the years before 1978, as this was the simplest hypothesis to backward extrapolate the survival data. However, it might be expected that survival figures improve over time before 1978 as occurred during the 1980s. The Danish Cancer Registry reported improvements in cancer patients’ survival for the major cancer sites [15] from 1943 to 1987, although no survival data is available for all cancer sites combined. We performed an additional estimation step with the assumption of increasing survival rates since 1950, with half of the rate estimated within the 1978–1989 period. This is equivalent to assuming a 10-year relative survival for females to decrease to 26% in 1950 from 39% as it was in 1980 (19 and 26% for males, respectively). The effect was negligible for estimated incidence. Prevalence, on the contrary, was moderately underestimated: by 15% in 1970, 6% in 1980, 1.5% in 1990, for females, and 11%, 3% and 1% for males, respectively.

Goodness of fit obtained by the MIAMOD method was very high, as it can be seen by the very small residuals shown by Fig. 2. Standard errors of incidence and prevalence estimates are generally quite small and not reported in the tables. Fig. 4 reports standard errors of cumulative risk of cancer to give an idea of the uncertainty of the estimates. Cumulative risk combines together incidence estimates for all ages during life, thus also combining uncertainties from each age-specific estimate. Although the age-specific standard errors are quite small, they become large when cumulated for individual ages up to 74 years. Standard errors of the estimates were derived as asymptotic estimates from the parameter covariance matrix, and they do not include the uncertainty deriving from a limited knowledge of the survival trends. For validation purposes, we applied the method to estimate incidence and prevalence for all cancers combined in the area of Varese covered by the Lombardy Cancer Registry (LCR). We estimated incidence in 1990 as 460 per 100 000 males and 350 per 10 000 females, where 503 and 387 is the published observed incidence [16] for males and females respectively, aged 0–84 years in that area. Our estimates, although approximately less than 10% lower than the observed rates, are consistent with the observation rates since the published incidence rates includes multiple primaries recorded by the CR, whereas estimates derived from mortality and survival strictly refer to individuals who experience cancer diagnosis for the first time. It was estimated that multiple primaries account for approximately 9–10% of cancers in the published LCR 1988–1992 figures. A different method that obtained nationwide estimates of incidence in the European countries [17], modelling the ratio of incidence/mortality using data from the cancer registries, estimated 115 114 and 95 363 new cancer cases in 1990

| Table 3 | Estimated trends in various indicators of life expectancy in Italy |
|---|---|---|---|
| Life expectancy (years) | Difference (years) |
| | 1990–1970 |
| Males | | | |
| Total | 68.9 | 73.7 | 74.4 | 4.8 |
| Cancer-free | 67.6 | 71.9 | 72.6 | 4.3 |
| Life with cancer | 1.3 | 1.8 | 1.8 | 0.5 |
| If death avoided | 71.5 | 77.7 | 78.3 | 6.2 |
| Females | | | |
| Total | 74.5 | 80.2 | 80.9 | 5.7 |
| Cancer-free | 72.5 | 77.7 | 78.6 | 5.2 |
| Life with cancer | 2 | 2.5 | 2.3 | 0.5 |
| If death avoided | 76.9 | 83.1 | 83.5 | 6.2 |

- Life expectancy at birth.
- Healthy life expectancy at birth with respect to cancer.
- Years of life expected to be lived with cancer for the population.
- Life expectancy at birth in the hypothesis that all cancers patients were cured, i.e. cancer eliminated as cause of death.
among Italian males and females, respectively. Our estimates provided very similar figures. We estimated in Italy, in 1990, 118,992 and 94,509 new cancer cases among males and females, respectively. Of course, neither of the two methods can be seen as a gold standard, as cancer registry data can be. Thus, comparing estimates by different methods can serve to show the variability of the estimates.

The projections were based on the assumption that the estimated effects of age and cohort on incidence persist during the projection period. Since we do not have data for patients diagnosed in the 1990s with complete long-term follow-up, no further improvements in survival were assumed after 1989, in the conservative hypothesis. In the optimistic hypothesis, we assumed that the observed survival trend in the period from 1978 to 1989 would continue after 1989. Projected incidence did not change when the two hypotheses were applied to the survival figures. Prevalence figures are projected to increase faster with the optimistic hypothesis, for both males and females. However, the range between the two hypotheses is quite small, representing 3 and 4% for males and females, respectively, in the year 2000. Projections appear to be rather robust to the moderate changes in survival rates in recent years. Although drastic changes in survival may occur, it is likely they occur as the result of new therapeutic and diagnostic strategies in specific cancer sites. The overall effect of these changes on the survival of all cancers combined being smaller.

To conclude, the data in this paper resulted in five major and related observations. First of all, the age-adjusted cancer mortality rates decreased since 1990 among females and were stable among males. Second, since 1990 the pattern of cancer incidence changed, starting to decrease for females and stabilising for males. Third, there was a generation effect, showing a reduction in the incidence rates for both males and females born after 1940. Fourth, there was an increase in the proportion of cured cancer patients with time. Finally, an increase since 1970 in both the total life expectancy at birth and the healthy life expectancy, i.e. the years of life expected for the population without any experience of cancer was observed.

The decline of age-adjusted rates of mortality and the changing pattern of cancer incidence, represent a great epidemiological transition that is going on in Italy. The decline in mortality is the combined effect of improvements in the survival of cancer patients and reduction of the risk of cancerous disease for the younger cohorts born after 1940. However, in spite of the reduction in the incidence rates, the number of cancer cases diagnosed annually will continue to increase, at a faster rate for males, due to the ageing Italian population.

The generation effect of the increase, i.e. seen in the older generation, and the subsequent reduction of the risk of cancer for the younger generations born after 1940 was also estimated to have occurred for the most frequent cancer sites in Italy, namely lung and larynx [10,18], breast [9] and colorectal cancers [12]. For stomach cancers [11,19], the reduction was found to be systematic and involving all generations and age classes. The decrease for these tumours accounts for most of the all-cancers decline.

Interpretation of the similar trend for all cancers combined is very difficult due to the multiplicity of diseases combined together. Great changes in smoking habits, nutritional factors, socio-economic and cultural factors occurred in Italy in the first half of the century, when industrialisation increased, poverty and deprivations spread due to entry into the First and Second World Wars. This situation reversed in the subsequent decades when there was a transition from an industrialised to a modern society, more involved in finance and services, including health services. Tobacco consumption started to decrease in males born after 1920–1930 and an increased availability of a wide variety of foods occurred in Italy in recent times. The increase and subsequent decrease of birth cohort cancer risk, is consistent with this changing pattern of Italian society, although not enough to substantiate the phenomenon.

The improvement in survival of cancer patients, reflects a general improvement in prognosis occurring for most cancer sites [2] and is to be interpreted as the result of a combination of many diagnostic and therapeutic improvements occurring in addition to the changing patterns of the major cancer sites. All of these factors resulted in an increased proportion of cured cancer patients, which was particularly marked for females (almost 20% increase for males, more than 30% for females). From an European study [20], it was observed that the main sites of incidence cases among Italian males were lung (21%), large bowel (13%), prostate (12%), bladder (7%) and stomach (7%) and in females (almost 20% increase for males, more than 30% for females). From an European study [20], it was observed that the main sites of incidence cases among Italian males were lung (21%), large bowel (13%), prostate (12%), bladder (7%) and stomach (7%) and in females were breast (28%), large bowel (15%), lung (6%), corpus uteri (5%) and stomach (5%). The changing pattern of incidence for the important cancer sites also affects survival for all cancers combined. Particularly, the decreasing trend of stomach cancer incidence [11] and the no longer increasing lung cancer incidence [10], for young generations born after 1940, are major factors influencing this favourable trend of cancer survival for males. The decreasing trend in incidence for stomach and cervix uteri cancer, and the increasing trend for female breast and lung cancers compete with each other in playing a role in determining an increase in the proportion of cured females with cancer, without any relevant increase in survival for not cured patients.

The total life expectancy and the healthy life expectancy, with respect to cancerous disease, increased in Italy from 1970 to 1990 and are expected to increase in the near future. Females have an expected life span after
cancer diagnosis that is longer than males. Although the years of life expected to be lived with cancer increased from 1970 to 1990, the projections to the year 2000 estimate that the number of years with cancer will no longer increase for males and will be decreasing for females. This could be the result of an increasing proportion of elderly patients whose survival is lower. The decrease in the years of life to be lived with cancer is an important epidemiological and demographic result, which supports the demographic theory of compression of morbidity, that is we are not only living longer, but also living longer in health, at least with respect to cancerous diseases. As an extreme hypothesis, if cancer patients were cured and cancer death prevented, males would gain a further 3.9 years of life expectancy, more than females, whose gain will be 2.6 years. Gain in life expectancy between 1970 and 1990 would be 6.2 years according to this hypothesis, both for males and females, thus eliminating the differential increase in life expectancy, 4.8 years for males and 5.7 years for females, experienced by the Italian population. Thus, cancer appears to be the factor responsible for the differential increase in life expectancy between males and females.

In the year 2000, there will be 239,000 Italians that will require treatment for a newly diagnosed cancer, 138,000 that will die from cancer and therefore require some form of terminal care. There will also be almost 57% of the one million plus people who had a diagnosis of cancer more than 5 years before, that will require either clinical assistance for recurrences or some form of clinical follow-up, although potentially less expensive depending on the time elapsed from diagnosis. Approximately 560,000 are the cases diagnosed within the 5 years up to 2000 and that require major health resources. Nearly 36% of the total female prevalence and 45% of the male prevalence contributed to this number.

The healthcare system has to face the expected growing cancer burden in the future. Prevention is the only action able to limit the occurrence of new cancer cases in the population and to avoid inducing further increases in cancer prevalence that also causes a great deprivation in quality of life in addition to an increased health demand. Devoting effort for a more incisive action against the diffusion of cigarette smoking, particularly for females, and toward promoting health dietary guidelines, are efficient ways to prevent a relevant proportion of respiratory and colorectal cancers. A lot of diagnostic and therapeutic resources could be saved by efficient prevention activities, such as the one for smoking habits occurring in the US, leading to a decline in lung cancer incidence since 1990 [21].

Finally, we have shown how the estimation of incidence and prevalence of all cancers combined is useful not only in giving information on the cancer burden, which is the basic information for planning and allocating resources in public health. Our analysis is also providing descriptive information of potential use for characterising the impact of cancer on the health status of the population.

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