The frequency of chronic conditions will continue to grow in the near future, as life expectancy increases and there is consequently a higher proportion of elderly people in the population. Data on occurrence and progression of diseases, such as incidence, survival, prevalence and mortality rates are essential to plan and implement major actions aimed at improving medical care services, and to evaluate the effects of public health interventions as well as spontaneously changing habits. To make a more thoughtful analysis not only should these figures be assessed for the past, but also for current and future years. Although widely available, mortality data are not exhaustive for the evaluation of the burden and the impact of disease. Incidence and prevalence are rarely available at national level and have to be estimated.

Among chronic diseases, cardiovascular disease and cancer represent the major health problems in industrialized countries and are important causes of death, morbidity and disability.

The aims of this study are (1) to reconstruct incidence and prevalence of major coronary events using the official mortality data and survival experience of coronary events provided by the Area Friuli-MONICA (MONItoring of CArdiovascular diseases) register, (2) to calculate projections for these from 1998 to 2007, and (3) to disentangle the trend in prevalence into its main determinants: population ageing, incidence trend, and survival trend.

The incidence and prevalence of major coronary events have been assessed using a statistical model named MIAMOD (Mortality and Incidence Analysis MODel). The model was

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**Estimating population-based incidence and prevalence of major coronary events**

S Giampaoli, L Palmieri, R Capocaccia, L Pilotto and D Vanuzzo

**Background**

Population-based data on coronary events are generally lacking for large areas, such as at the nation-wide level. While mortality data are currently and exhaustively collected in all developed countries and in a few developing countries, incidence and prevalence are often available only for certain subgroups of the population under study.

**Methods**

We propose to estimate population-based incidence and prevalence of coronary events through a mathematical method using mortality and survival data as input, and to forecast coronary event occurrence using an age, period and cohort approach. The method reconstructs incidence and prevalence of major coronary events in Italy from 1970 to 1997 and projects trends up to the year 2007 using survival data on coronary events from the Area Friuli-MONICA (MONItoring of CArdiovascular diseases) register.

**Results**

Major coronary event incidence has been decreasing since 1977 for men and since 1974, for women. Conversely, major coronary event prevalence increased up to the end of the 1980s for men and up to the early 1980s for women, and it has been declining thereafter. Major coronary event prevalence results from three main effects: increasing survival, population ageing, and incidence trend.

**Conclusions**

Availability of national population data, collection of population-based survival data from the MONICA registers and appropriate statistical and mathematical methods help to estimate and project incidence and prevalence trends for major coronary events. This information is essential to plan and implement actions aimed at improving medical care services, and to evaluate the impact of public health interventions as well as spontaneously changing habits.

**Keywords**

Incidence, prevalence, mortality, projections, ischaemic heart disease, coronary events

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applied in Italy at the beginning of the 1990s as a pilot analysis using survival and 3-year incidence from the Area Latina-MONICA project.3

Methods
Healthy individuals are conventionally assumed to become incident cases at the date of diagnosis of an event. Incident cases are considered prevalent until death.

For each dead person, the date of diagnosis can be reconstructed as the difference between time of death and survival time. Similarly, in populations, incidence rates can be computed by age and period, using mortality data and assuming an appropriate distribution of survival times (Figure 1).

Major coronary events and survival time are provided by the Area Friuli-MONICA register. Official population and mortality data at national and regional level derive from the 'Istituto Nazionale di Statistica' (ISTAT). Cases diagnosed with major coronary events can die of causes unrelated to ischaemic heart disease. This has been accounted for by using relative survival, which is calculated as the ratio of survival rate assessed in the patients and that in a general population assumed to be similar to the patients except for the illness under study.4 Observed survival has been calculated by the actuarial method.5

The MIAMOD model is based on the mathematical relationship between mortality, morbidity and survival from chronic diseases.6 Disease incidence probability is assumed to be a continuous function of age, period, birth cohort and a set of parameters.

A polynomial function of age and cohort of birth and a set of ‘cubic spline’ functions7 of year of diagnosis in logistic scale have been considered to model incidence rates in different age groups and periods. Model parameters are coefficients of age, cohort and period variables; they completely determine the incidence function at each age and period. Parameters are estimated using the mathematical relationships holding among incidence, prevalence, survival and mortality when a chronic disease is assumed to be irreversible. A system of two integral equations relates incidence and prevalence of a cohort to its general and specific mortality cause and to survival rates.8 General and specific mortality cause rates are available for each age class and for each year; if survival rates are assumed to be known, and the above mentioned equation system is used for each involved birth cohort, it is possible to express the expected specific mortality rates as a function of the unknown set of parameters. Parameters of incidence function are estimated as the best reproducing observed mortality data. The probability of observing deaths at each age class and calendar year from corresponding person-year at risk is assumed to be Poisson distribution with expectation as function of the mid-points of the considered age class and time period. The maximum likelihood estimates of parameters are obtained by an iteratively reweighted least squares procedure, minimizing with respect to parameters the residual variance of number of deaths; weights are the inverse of the variance of deaths for each age class and calendar year.

Goodness-of-fit is evaluated by the likelihood ratio statistic (LRS). The order of polynomials and the number of knots chosen between 1970 and 1997, used in the incidence function, is based on the LRS test.9 Standard errors of maximum likelihood estimates are obtained from the second derivatives of the likelihood function and standard errors of incidence and prevalence estimates are derived.1

Once parameters have been estimated, incidence function provides the basic tools for calculating projections of future coronary event occurrence. Projected incidence rates are based on the hypothesis that estimated incidence function, birth cohort cumulative risk and incidence trend by age will continue to hold in the future. Incidence rates are estimated by extending the application to the forecast period. Age and birth cohort factors maintain the same estimated polynomial function in the projection; period factor is instead linearly projected by a gradient estimated choosing the last 10 years trend from the estimation period. The convenience of the age, period and cohort approach in projecting the disease trend, compared to the more traditional method of interpolation and extrapolation of a time-trend series, has been recognized in previous articles dealing with mortality projections.9,10 Cohorts that will be born during the forecast period are not considered in the projections. Prevalence and specific mortality cause rates have been projected from projected incidence and survival rates.

A complete description of the MIAMOD method and software, widely implemented and used for cancer studies, is reported in Verdecchia et al.,8 and De Angelis et al.1,2

Data regarding major coronary events were obtained from the Area Friuli-MONICA Project, a surveillance system for coronary events covering a North-eastern region of Italy and including men and women aged 25–64 years with a first coronary event from 1984 to 1993.

In this analysis fatal and non-fatal events have been selected according to MONICA criteria11: fatal coronary events as ‘definite’, ‘possible’ and ‘insufficient data cases with ischaemic heart disease as first cause of death’ and non-fatal coronary events as ‘definite’ or ‘cardiac arrest with successful resuscitation’. For each subject only the first coronary event recorded in 10 years of surveillance has been included. Events have been followed-up for mortality until 31 December 1997. Potential survival time ranges between 4 and 13 years. Long-term survival is computed as the time from the first major coronary event to the time of death or the end of the follow-up. Survival data include 5462 incident cases (4512 men and 950 women aged 25–64 years). The target population included approximately 662 000 people (about 2.2% of the Italian population). Survival estimates for patients aged 25–64 years have been extrapolated to patients 65–74 years old in order to extend the analysis to a wider set of population and mortality data.

For this purpose survival ratios between the age groups 55–64 and 65–74 years, obtained from the data of the Area Latina-MONICA Project,3 have been applied to the same age groups in the Area Friuli for each diagnosis period. The Area Latina-MONICA register considered coronary events that occurred between 1983 and 1985 among residents in a region of Central Italy and they were followed-up to June 1992. The median values of extrapolated annual age survival from 65 to 74 in each

![Figure 1](natural-history-of-a-chronic-disease.png)
period have been used as representative of survival among related age groups in the Area Friuli. Long-term relative survival rates for cases diagnosed 1990–1993 have been assessed as the product of independent conditional relative survival rates obtained by a linear regression model estimated on the basis of available previous times. Survival rates by age and sex have been considered constant before 1984 and after 1993 since no other data were available outside the MONICA register period.

Official mortality data with Codes 410 'acute myocardial infarction', 411 'other acute and subacute forms of ischaemic heart disease', 412 'old myocardial infarction', 413 'angina pectoris' and 414 'other forms of chronic ischaemic disease' are included. Population and mortality data are obtained from national official statistics by sex, age and calendar year from 1970 to 1997.

Changes in prevalence are due to three main effects: increasing survival, population ageing and incidence trend. We have quantified the first effect by comparing estimated prevalence with a similar estimate obtained under constant survival rates. The second component has been estimated comparing crude and age-adjusted prevalence. Finally, the third effect has been obtained as the difference between total changes and the sum of the other two components. Increasing survival causes patients to remain in a state of illness for a longer period producing a growth in prevalent cases; population ageing allows people, surviving patients included, to live longer with a similar result in growth of prevalence; a decreasing incidence trend provides fewer coronary events and consequently fewer prevalent cases. The opposite effects of these components on prevalence persisting over a period of time produces an increased or decreased number of prevalent cases at the end of the period.

Results

Figure 2 shows age-adjusted estimated and projected mortality for ischaemic heart disease and the estimated and projected incidence trend for major coronary events in men aged 25–74 years. Both the incidence and mortality curves are presented, firstly assuming that survival is constant during the 10 years of Area Friuli-MONICA register, and secondly assuming that survival follows the temporal dynamic observed in the same period. Since the observed survival has improved during the surveillance period, the assumption of constant survival rates causes a reduction in the number of new cases sufficient to reproduce mortality and leads to lower incidence rates. Rates have been age-adjusted in order to allow comparison over the whole period of estimation and projection.

The estimation covers the period 1970–1997 and constitutes the basis for projection for the period 1998–2007. As official mortality, incidence rates increase until the middle of the 1970s, steeply decline until the first half of the 1980s, and then slowly and steadily decrease until the end of the projection period.

Figure 3 shows the same trends for women; incidence and mortality trends are closer to each other than those for men due to the lower survival of women, but the overall pattern is similar. The MIAMOD model allows the calculation of standard errors of incidence for each age group taking into account the variability of mortality rates. In all cases standard errors are less than 1% of the corresponding incidence rates; such variability can be considered negligible and is not represented in the Figure.

Table 1 reports estimated and projected incidence rates from 1970 to 2007. In the last year of the projection about 27 200 new male cases and about 9500 new female cases of major coronary events are forecast, with age-adjusted rates of 128.3 per 100 000 and 42.6 per 100 000, respectively.

Table 1  Estimated incidence of major coronary events in Italy, 25–74 years of age

<table>
<thead>
<tr>
<th></th>
<th>Men</th>
<th>Women</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>38 075</td>
<td>46 145</td>
</tr>
<tr>
<td>Crudea</td>
<td>258.2</td>
<td>293.4</td>
</tr>
<tr>
<td>AARb</td>
<td>258.2</td>
<td>281.0</td>
</tr>
</tbody>
</table>

a Crude rate (<100 000).
b Age-adjusted rates (<100 000).
Table 2 shows estimated prevalence for the year 1997 and projections to the year 2007. In this period prevalent cases decrease from 227,000 to 191,000 in men and from 41,000 to 35,000 in women.

This is the result of the contrasting effects provided by the different components. For men, the decreasing prevalence can be disentangled into an increment of about 53,000 cases due to improvement in survival, 62,000 cases due to population ageing, and a reduction of about 151,000 cases due to the effect of declining incidence trend. For women, lower prevalence results from an increase of 9,900 cases attributable to improved survival, about 10,200 cases due to population ageing and a reduction of about 25,000 cases due to the effect of decreasing incidence trend.

Therefore, in both genders, a strong decreasing trend of incidence, not completely balanced by the effects of survival improvement and population ageing, produces a reduction of prevalent cases in 10 years. The three main effects explaining prevalence changes between 1997 and 2007 may also give an idea of the sensitivity of the model under different assumptions. The increased number of prevalent cases, due to an improving survival, indicates the number of deaths occurring under the assumption of a steady survival during the 10 years. The increased number of prevalent cases, due to population ageing, indicates the number of sick subjects added to the estimate in comparison to the result obtained under the assumption of a steady population in the same 10 years. Finally, the decreased number of sick people, due to the decreasing incidence, reflects the hypothetical number of patients that could be acquired under the assumption of a steady incidence in the same period.

### Discussion

The MIAMOD method has been used in cancer modelling.\(^8,13–16\) The general approach depends on two hypotheses: (a) the disease is irreversible, and (b) incidence can be expressed as a continuous function of age, period and cohort. Such hypotheses are reasonable because: (a) subjects surviving a first coronary event have a higher risk of another coronary event than healthy people and require special resources from health services; (b) there is no biological reason for sudden incidence increases with respect to the age, period and cohort variables.

The MIAMOD model applied in this analysis is basically the same as that used in previous work relating to Area Latina-MONICA Project published by Frova et al. in 1997,\(^3\) but some important differences have to be stressed. In the previous work only 3-year survival data from Area Latina-MONICA register (basically constant values) were used to implement the model, whereas here 10-year survival from the Area Friuli-MONICA register, a wider region than Area Latina, in addition to previous data, provide a more accurate and reliable description of the temporal dynamic of survival information. From a methodological point of view the main difference relates to functions used in period effect estimation: a set of cubic splines instead of a polynomial function represents a more flexible way to describe and reconstruct non-linear trends. Finally updated mortality and population data until 1997, confirming trends of previous years, enable projection of incidence and prevalence up to 2007 and production of more reliable results.

Relative survival rates were calculated by age and gender from data collected by the Area Friuli-MONICA Project from 1984 to 1993. Survival quickly decreases in the first 6 months after the event, basically due to death in the first 28 days. In the following periods survival curves almost flatten, meaning that patients’ mortality approaches that of the healthy population. Young men (35–54 years) show a better survival than older men. Women do not show survival differences by age. This result in women is probably due to the age cut of 64 years which excludes ages where cases are more frequent. Survival improved from the first to the second half of the 1980s. This trend can be interpreted as a consequence of innovative therapies in the acute phase of the event.

The survival rates estimated for incident cases in the Area Friuli have been taken as representative of major coronary event survival probability for the Italian population aged 25–74 years. Limiting the comparison at the first 3 years of follow-up, we have compared Friuli data with those from the Area Latina for the period 1983–1985.\(^3\) The observed survival rates in the two areas, at 3 years from diagnosis, do not differ significantly. Survival in men aged 25–44 years is 0.60 in the Area Latina and 0.57 in the Area Friuli; in men aged 45–54 survival rates are 0.59 in both areas and, in men aged 55–64 survival rates are 0.43 in both areas. In women, survival rates are 0.43 in the Area Latina and 0.49 in the Area Friuli for the age group 25–44; 0.40 in the Area Latina and 0.49 in the Area Friuli in the age group 45–54; and, finally, 0.30 and 0.42, respectively, in the Area Latina and in the Area Friuli in the age group 55–64 years. Such survival similarity gave us the confidence to use the survival trend between the last two age groups (55–64 and 65–74) from the Area Latina-MONICA Project to extrapolate missing survival rates in the 65–74 age group of the Area Friuli-MONICA Project. The survival age trend has been applied starting from the 55–64 survival rate in each of the three periods 1984–1986, 1987–1989.
and 1990–1993. In this way the survival period characteristics in the Area Friuli project have been maintained.

The Area Friuli register is population-based including in- and out-of-hospital cases; in contrast, hospital-based studies usually cover only events reaching hospital; for this reason clinical data show better survival rates for coronary events and are scarcely comparable to population-based survival studies. Compared with longitudinal studies, the register covers a wider population, but non-fatal events occurred outside the surveillance area and clinical silent myocardial infarction are not included; longitudinal studies usually involve small population samples and permit to collect information on silent myocardial infarction and non-fatal events occurred outside the area.

Even though a certain degree of misclassification of cause of death certainly exists, we believe that taking into account mortality codes as 410–414 in official death records is the best approximation of the fatal major coronary events.

We have compared mortality rates from Italy and the Friuli region by sex from 1970 to 1997: both the Friuli and the Italian mortality trends for men and women are similar; Friuli mortality rates present slightly higher figures with a maximum difference of 0.05% in 1976. From this year onward mortality rates difference declines and basically overlap from 1984 in men and from 1988 in women.

To validate the assessed figures described in this paper we have compared the prevalence rates obtained using the MIAMOD, with those collected within the Osservatorio Epidemiologico Cardiovascolare (OEC), a survey at national level carried out during 1998 in randomly selected samples of more than 6000 men and women aged 35–74 years. In the OEC the estimated prevalence of major coronary events assessed by the history of myocardial infarction and specific ECG Minnesota Code findings was 0.75% among men 45–54 years (0.78% in the MIAMOD model), 2.53% in the 55–64 age group (2.42% in the MIAMOD model) and 4.73% in the older age group 65–74 years (4.36% in the MIAMOD model). Unfortunately, given the scarce number of events in the age groups covered by the OEC, it has not been possible to compare estimates for incidence and for women.

A different model has been used in a cohort study carried out by the Australian National Centre for Epidemiology and Population Health to simulate individuals’ coronary heart disease history up to 2014 for a sampled Australian population (aged 45–69 years) characterized by major coronary risk factors and to project hospital costs associated. Their results about treatment efficacy as a whole and not specifically.

Comparison with observed OEC data make us confident to produce sufficiently good prevalence and incidence estimates and projections. In the year 2000 the project ‘National Registry of the Cardiovascular Diseases’ has started in seven centres homogeneously distributed on the national territory. Results from this project will hopefully provide a wider and accurate estimation of national major coronary event survival and consequently will help to estimate more reliable incidence and prevalence projections.

Usually only mortality data are available at national level; this application is a further use of data from registries, which, combined with official population and mortality data, could help to provide reliable estimates and projections of incidence and prevalence at national level, supplying wider and more comprehensive information to plan public health resources and interventions.

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