Incidence and prevalence of ischemic heart disease in Italy: estimates from the MIAMOD method

Simona Giampaoli, Luigi Palmieri, Lorenza Pilotto*, Diego Vanuzzo*

*Laboratory of Epidemiology and Biostatistics, Istituto Superiore di Sanità, Rome, *Center for the Prevention of Cardiovascular Diseases, ASS4 Medio Friuli, Agenzia Regionale della Sanità, Udine, Italy*

Key words:
Epidemiology; Ischemic heart disease.

Background. **When considering large areas, population-based data on coronary events are generally lacking, and such is the case for the national level. While mortality data are currently and exhaustively collected, data regarding the incidence and prevalence are often available only for subgroups of the population.**

Methods. **The incidence and prevalence of coronary events were estimated using a mathematical method on the basis of official mortality and population data from national statistics and survival data on coronary events from the Area Friuli of the MONICA Project, and forecasted for northern, central and southern Italy.**

Results. **The incidence is described from 1970 to 1994 and projected to the year 2004; prevalence is reported at the years 1990 and 2000. The coronary event incidence has been decreasing since 1977 among men and since 1974, 4 years before the observed mortality decline, among women. The prevalence has continued to increase as a result of three main factors: increasing survival, population aging, and incidence trend.**

Conclusions. **Incidence and prevalence data distributed for northern, central and southern Italy are essential to plan and implement major projects aimed at improving medical care services and to evaluate the impact of public health interventions and of spontaneously changing habits among the population.**

(Ital Heart J 2001; 2 (5): 349-355)

This research was partially supported by "Il Progetto CUORE - Epidemiology and prevention of ischemic heart disease" funded by the Italian Ministry of Health.

Received July 10, 2000; revision received December 15, 2000; accepted January 25, 2001.

Address:

Dr.ssa Simona Giampaoli

Laboratorio di Epidemiologia e Biostatistica
Istituto Superiore di Sanità
Viale Regina Elena, 299
00161 Roma
E-mail: sgiamp@iss.it

Introduction

It is expected that in the near future, the number of individuals exposed to cardiovascular disease will continue to increase. This is due to the fact that for a given age, life expectancy is longer and consequently a more relevant proportion of the population consists of elderly people. Data on the occurrence and progression of diseases, such as the incidence, survival, prevalence and mortality rates are essential to plan and implement major projects aimed at improving medical care services, and to evaluate the effects of public health interventions as well as spontaneously changing habits among people. To elaborate a more rational analysis these figures should be assessed not only for the past, but also for the current and the next 3-5 years. Although widely available, mortality data are not exhaustive for the precise evaluation of the burden and impact of diseases. The national incidence and prevalence are rarely available and consequently have to be estimated.

The aim of this study was to reconstruct the incidence and prevalence of coronary events for northern, central and southern Italy, to calculate projected incidence and prevalence trends for the decade 1995 to 2004 using the official mortality and the survival experience of coronary events in the northern part of Italy covered by the Area Friuli Register of the MONICA Project and to subdivide prevalence data into its determinants, that is increasing survival, population aging, and incidence trend.

The incidence and prevalence of major coronary events have been assessed by a statistical model named MIAMOD (Mortality and Incidence Analysis MODel)[1-3].

Methods

A complete description of the MIAMOD method and software is reported by Verdecchia et al.[4] and De Angelis et al.[1,2]. The method applied for estimating incidence and prevalence is based on the mathematical re-

lationship between mortality and morbidity and surveillance of chronic diseases[5]. A polynomial function of age and year of birth (cohort) and a set of "cubic splines" functions[6] of year of diagnosis (period) in the logistic scale have been considered for modeling incidence rates in different age groups and periods. Coefficients of age, cohort and period variables are the model parameters. They completely determine the incidence function at each age and period. The adequacy of fit is evaluated by the likelihood ratio statistics.

Once the parameters have been estimated, the incidence function provides the basic tools for projection of future coronary event occurrence[7,8]. Projected incidence rates are based on the hypothesis that the 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. Two assumptions are necessary: 1) age and birth-cohort effects have to remain the same as those estimated for the past, 2) future incidence levels are not to be influenced by non-linear period effects.

Diagnostic criteria defining the coronary event were selected according to the MONICA criteria[9] as follows: a fatal coronary event was classified as a definite or possible coronary event, or insufficient data with fatal ischemic heart disease (International Classification of Diseases, IX revision - ICD IX 410-414) as the first cause of death; on the other hand, a non-fatal coronary event was classified as a definite coronary event or cardiac arrest with successful resuscitation. Incident events were considered prevalent until death.

According to the ICD IX, code 410 includes "acute myocardial infarction", code 411 includes "other acute and subacute forms of ischemic heart disease", code 412 includes "old myocardial infarction", code 413 includes "angina pectoris", and code 414 includes "other forms of chronic ischemic disease".

The time of death can be calculated if the date of the event and the survival time are known. Similarly, the date of the event (time-point) and incidence can be computed when the time of death and survival are known. Incidence rates can be estimated using mortality data and assuming an appropriate distribution of survival time.

Population and mortality data from national official statistics by sex, age and calendar year from 1970 to 1994 and survival rates observed in the MONICA Project-Area Friuli, for subjects aged 25-64 years with a first coronary event that occurred from 1984 to 1993 (subdivided in the periods 1984-1986, 1987-1989 and 1990-1993), were included in the MIAMOD application. The long-term survival was computed as the time from the first coronary event to the time of death or the end of follow-up (December 1997). Survival data included 5462 incident cases (4512 men and 950 women aged from 25 to 64 years). The potential survival time ranged between 4 and 13 years. The survival data of patients from 25 to 64 years of age have been extended to patients 65-74 years old for coherence with available population and mortality data.

The annual age trend of survival between the age group 55-64 and the age group 65-74 years, derived from the data of the MONICA Project-Area Latina[3], has been applied to the age groups 55-64 years of each period (1984-1986, 1987-1989 and 1990-1993) in order to estimate survival rates for patients aged 65-74 years in the Area Friuli. The median values of the extrapolated annual age survival of the age group 65 to 74 years in each period have been used as the representative survival of the related age groups in the Area Friuli. With regard to the last period (1990-1993), the cumulated relative survival probabilities were not always available in the last times from diagnosis; they have been reconstructed as the product of independent relative survival rates obtained by a linear regression model.

The relative survival has been calculated as the ratio between absolute survival in the patients' group and that in the general population assumed to be similar to the patients' group with the exception of the illness under study[10]. The absolute survival has been calculated by the actuarial method[11].

Projections were made for the decade 1995 to 2004 by sex and ages (25 to 74 years); projections for ages before 25 and after 74 years were not considered such that results were steady and reliable. Changes in prevalence cases between the years 1990 and 2000 were due to the effects of three main factors: increasing survival, population aging and incidence trend; we have quantified the first effect by comparing the estimated prevalence of constant and dynamic survival rates, the second by comparing the estimated prevalence of the actual population and a steady population from the year 1990 onwards, and the third as the difference between total changes and the other two components.

There are three main components which influence changes in prevalence: increasing survival results in prolonged illness and thus in growth of prevalent cases; population aging results in increased longevity for everyone, survivors included, with a similar result in prevalence growth; a decreasing incidence trend means less coronary events and consequently less prevalent cases. The opposite effects of these components on prevalence ongoing during a period of time produce an increased or decreased number of prevalent cases at the end of the period. Tables I and II describe the differences in prevalent cases due to these three effects.

Italy has been subdivided in three main geographic areas: northern, central and southern. According to the ISTAT (Italian National Institute of Statistics) the northern area includes the regions of Piemonte, Valle d'Aosta, Lombardia, Liguria, Veneto, Friuli Venezia Giulia, Trentino Alto Adige, and Emilia Romagna; central Italy includes Toscana, Lazio, Umbria and Marche whereas Abruzzo, Campania, Molise, Calabria, Puglia, Basilicata, Sicilia, and Sardegna belong to southern Italy.

Table I. Number of prevalent cases of coronary events by geographic area in men aged 25-74 years. Changes during the period 1990-2000.

	Italy		North		Center		South	
	Cases	ASR × 10 000	Cases	ASR × 10 000	Cases	ASR × 10 000	Cases	ASR × 10 000
Year 1990	217 597 (100%)	129.4	113 784 (100%)	144.0	40 601 (100%)	115.2	62 632 (100%)	116.3
Year 2000	220 183	113.9	107 764	117.1	41 940	106.3	70 095	113.2
Difference	2586 (1.2%)		-6020 (-5.3%)		1339 (3.3%)		7463 (11.9%)	
Due to increasing survival	26 838		19 576		4362		2730	
Due to population aging	51 416		69 577		39 206		32 256	
Due to incidence trend	-75 668		-95 174		-42 229		-27 523	

ASR = age standardized rates obtained using the Italian population in 1990.

Table II. Number of prevalent cases of coronary events by geographic area in women aged 25-74 years. Changes during the period 1990-2000.

	Italy		North		Center		South	
	Cases	ASR × 10 000	Cases	ASR × 10 000	Cases	ASR × 10 000	Cases	ASR × 10 000
Year 1990	39 104 (100%)	21.9	18 720 (100%)	21.9	6829 (100%)	18.5	13 541 (100%)	24.2
Year 2000	43 263	20.8	19 344	19.5	8056	18.9	15 818	23.8
Difference	4159 (10.6%)		624 (3.3%)		1227 (18.0%)		2277 (16.8%)	
Due to increasing survival	4233		2306		355		916	
Due to population aging	9087		10 685		5886		8890	
Due to incidence trend	-9161		-12 368		-5014		-7529	

ASR = age standardized rates obtained using the Italian population in 1990.

Results

Figure 1 shows relative survival by sex and age in the MONICA-Area Friuli. Survival rapidly decreased of an amount ranging between 40 to 50% in the first 6 months after the event. This figure was basically due to deaths occurring in the first 28 days. In the following periods survival curves showed a steady trend meaning that survival did not get worse. Young men (from 35 to 54 years old) showed a better survival than older men; women did not show survival differences; this result in women is surely due to the age limit of 64 years which excluded age groups with the highest prevalence of cases. Figure 2 shows survival by event period (1984-1986, 1987-1989 and 1990-1993): an increase in survival is evident from the first to the second half of the ’80s.

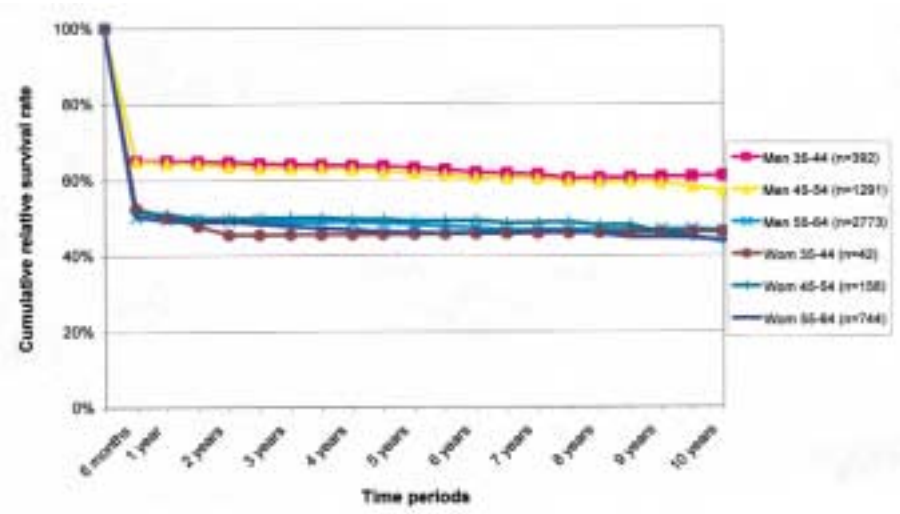

Figure 1. *MONICA Project-Area Friuli: relative survival curves by age (35-64 years) of male and female patients.*

This was definitely due to the introduction of innovative therapies for the acute phase of the event.

Figure 3 shows the age-adjusted estimated and projected mortality for ischemic heart diseases (ICD IX 410-414) and the estimated and projected incidence trends for coronary events (MONICA criteria) among men aged 25-74 years for the whole of Italy and for the northern, central and southern regions separately. The estimates covered the period 1970-1994 and constituted the basis for the projection of data regarding the period 1994-2004. As for official mortality, incidence rates increased until the middle of the '70s. A steep decline until the first half of the '80s then occurred and was followed by a slow and steady decrease until the end of the projection period. As for mortality, in the middle of the '70s, the rates were higher in northern compared to central and southern Italy, while at the end of the '90s these differences among areas appeared completely flattened.

Figure 4 shows trends for women: due to the lower survival of women, incidence and mortality trends were closer to each other than those for men but the overall pattern was quite similar. Among women the difference in incidence rates between northern and central and southern regions reported for the '70s are completely flattened at the beginning of the '90s.

The MIAMOD method allows calculation of standard errors of incidence for each age group on the basis of parameters estimated for age, period and cohort. In each implementation, both in men and women, total standard errors were between one and three thousandths of the incidence; such variability could be considered negligible.

Table III reports the number of new coronary events and incidence rates projected to the year 2000. Considering the whole of Italy, this would amount to approximately 37 000 new cases among men; using the model separately for the northern, central and southern regions,

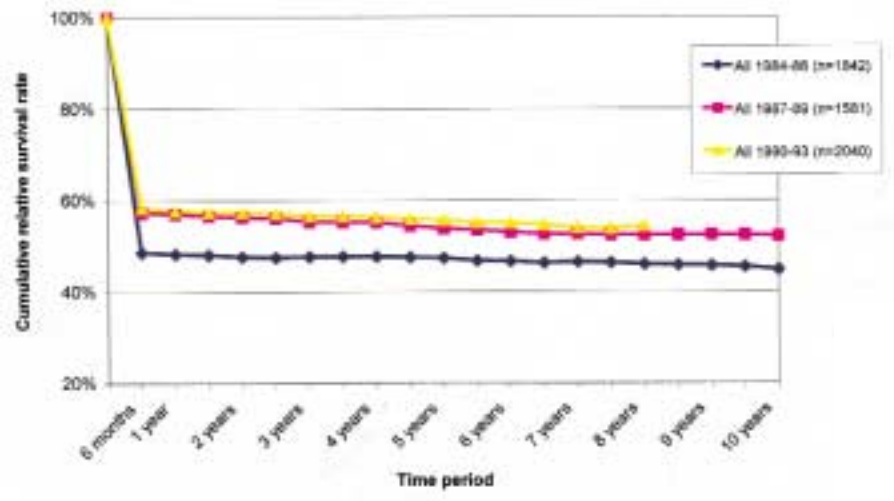

Figure 2. *MONICA Project-Area Friuli: relative survival curves by joining period for all sexes and ages (35-64 years).*

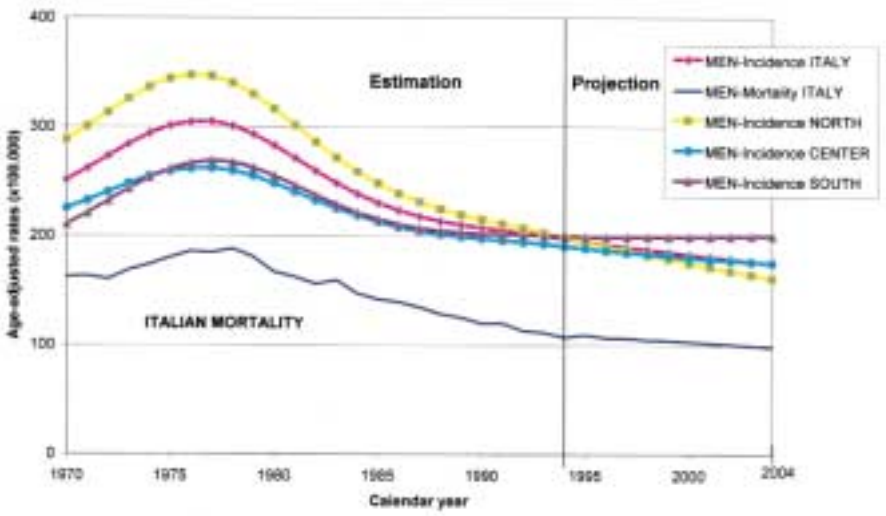

Figure 3. *Incidence of major coronary events in Italy by geographic area; men aged 25-74 years, 1970-2004.*

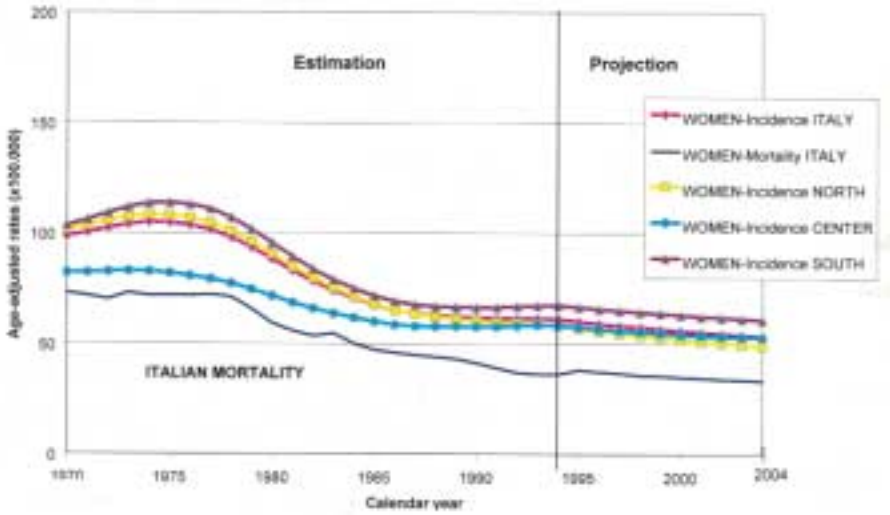

Figure 4. *Incidence of major coronary events in Italy by geographic area; women aged 25-74 years, 1970-2004.*

Table III. Major coronary events: estimated incidence rates in Italy to the year 2000 by geographic area; 25-74 years of age.

	Men				Women			
	Italy	North	Center	South	Italy	North	Center	South
Cases	36 573	16 649	7325	12 820	12 177	5381	2426	4379
ASR (× 100 000)	182.7	175.0	179.8	199.3	55.7	51.7	54.0	62.9

ASR = age standardized rates obtained using data of the Italian population in 1970.

the estimated new cases were as follows: about 17 000, 7000 and 13 000 for northern, central and southern Italy respectively. With regard to women, the national estimate was about 12 000 new cases including approximately 5000, 2000 and 4000 for northern, central and southern Italy respectively. Rates have been standardized using data of the Italian population at the beginning of the estimation period (1970): the age-adjusted incidence rates were about 183 per 100 000 and 56 per 100 000 for men and women respectively. Considering the regions separately and comparing the respective data to national estimates, the age-adjusted incidence rates both for men and women were higher in southern and central Italy and lower in northern Italy.

Table I shows both the estimated number of prevalent cases and the corresponding age-adjusted prevalence rates for the year 1990 and their projections to the year 2000 among men (rates have been standardized by direct method using data of the Italian population in 1990 as reference). In Italy prevalent cases increased from about 218 000 in 1990 to almost 220 000 in the year 2000; this was the result of the contrasting effects of different components: the slight increase in prevalent cases (1.2%) was obtained by summing up the effects of increasing survival and population aging (increment) and of declining incidence (decrement). In spite of the absolute increase in the number of prevalent cases of coronary events, the age-adjusted prevalence rate decreased from 129.4 per 10 000 in 1990 to 113.9 per 10 000 in the year 2000. This was due to the increase in the Italian population in the same period.

Partitioning these data by geographical area, in northern Italy an almost 5.3% reduction in prevalence was evident. This is attributable to the fact that the significant decrease in prevalent cases related to the incidence trend was not compensated by the increase in prevalent cases related to the effects of better survival and population aging. Even though the effects of these components on prevalence follow the same trend both in the Center and in the South, the number of prevalent cases in these areas increased by about 3.3 and 11.9% respectively. Obviously the percentage effects are to be matched to the absolute numbers indicated in table I and to the resident population which we know to be greater in the North as compared to that in the Center and in the South. So, in the northern area, the age-adjusted prevalence rate decreased from 144.0 per 10 000 in 1990 to 117.1 per 10 000 in the year 2000; in the Center the prevalence rate decreased from 115.2 to 106.3 per 10 000 whereas in the southern area, it decreased only slightly from 116.3 to 113.2 per 10 000.

Table II shows the estimated number of prevalent cases for the year 1990 and projections to the year 2000 among women. In Italy prevalent cases increased from about 39 000 in 1990 to 43 000 in the year 2000. The 10.6% increase in the number of prevalent cases was ob-

tained by summing up the effects of improved survival and population aging (increment) and those due to the decreased incidence of new cases (decrement). In the northern area the prevalence remained almost unchanged (3.3%) as a result of the fact that the negative contribution by the decreasing incidence was well compensated by the positive effect of increasing survival and population aging. In central and southern Italy the number of prevalent cases increased by 18.0 and 16.8% respectively. In northern Italy, the age-adjusted prevalence rate decreased from 21.9 per 10 000 in 1990 to 19.5 per 10 000 in the year 2000; in central Italy the prevalence rate remained almost unchanged and increased only slightly from 18.5 to 18.9 per 10 000; in the South a slight decrease (from 24.2 to 23.8 per 10 000) occurred.

Therefore, with regard to national data, in both genders a positive 10-year contribution to prevalent cases by improved survival and population aging resulted in only a slight increase in the number of prevalent cases due to a compensatory effect by the decrease in incidence. This result was the sum of the positive contribution by the number of prevalent cases from central and southern Italy and of the negative net contribution (lower positive in women + negative in men) from the northern area.

In the three geographical areas of the country the same results in terms of the absolute number of prevalent cases corresponded to a general decrease in the age-adjusted prevalence rates from 1990 to the year 2000 in both genders.

Discussion

The MIAMOD method has been widely used to provide estimations and projections of cancer incidence[4,12-15]. This modeling approach depends on two assumptions: a) the disease is assumed to be irreversible, and b) the incidence is expressed as a continuous function of age, period and birth cohort.

Such assumptions are reasonable as: a) in view of the fact that survivors of a first coronary event have a higher risk of recurrences than healthy people and consequently require special resources from health services, these patients are considered prevalent cases for the rest of their life span; b) the incidence depends on age, period and birth cohort which are continuous time-related variables.

The survival rates estimated for incident cases in the Area Friuli of the MONICA Project have been taken as representative of coronary event survival probability for the Italian population aged 25-74 years. Limiting the comparison to the first 3-year follow-up, we have compared the Area Friuli data with those of the Area Latina of the MONICA Project in central Italy, in the period 1983-1985[3]: the observed survival rates of the two areas were quite similar.

Such a survival similarity constituted the basis of our rationale in using the survival trends of the last two age groups (55-64 and 65-74 years) from MONICA-Area Latina to extrapolate lacking survival rates in the 65-74 year age group of MONICA-Area Friuli. The survival age trend has been applied beginning from the survival rate of the 55-64 year age group in each of the three periods 1984-1986, 1987-1989 and 1990-1993. In this way the survival period characteristics in the Area Friuli have been held.

To validate the assessed figures described in this paper we have also compared the prevalence rates obtained using the MIAMOD for 1994, the last year with available national official mortality data, with those collected by the Italian Osservatorio Epidemiologico Cardiovascolare (OEC) during 1998 in randomly selected samples disseminated throughout the whole country and totaling more than 6000 individuals aged 35-74 years. Among men aged 55-64 years, the estimated prevalence of ischemic heart disease according to the OEC (derived from the history of myocardial infarction and specific electrocardiographic findings read by the Minnesota Code) and that obtained using the MIAMOD, were very similar (OEC 0.253%, MIAMOD 0.256%). The same applied for the 65-74 year age group (OEC 0.473%, MIAMOD 0.454%). Unfortunately, given the scarce number of events among females in the age groups covered by the OEC, it has not been possible to compare estimates for women.

In view of these results, we are confident that our prevalence and incidence estimates and projections are sufficiently reliable. However, more survival data from registries distributed throughout the country could help to produce more appropriate estimates. In the year 2000 the project “National Registry of the Cardiovascular Diseases”, including 2-year retrospective registries of cardiovascular diseases, has started in seven centers homogeneously distributed in the national territory. Results from this project will surely provide a wider and more accurate estimation of national coronary event survival and consequently will help to estimate incidence and prevalence projections more reliably.

The Area Friuli of the MONICA Project collected population-based data of acute myocardial infarction, including in- and out-of-hospital cases; in contrast hospital-based studies usually cover only those patients who reach the hospital; for this reason hospital data show a better survival rate for coronary events. However, they are of little use in the planning and implementation of major projects aimed at evaluating and improving public health interventions and services[16].

Our approach based on the data from the MONICA Register in a limited area representative of the country, gives the opportunity of providing incidence and prevalence estimates and projections at the national level. These are fundamental for planning the public health requirements of the country. The model allows to disentangle prevalence changes into its three main compo-

nents, i.e. increasing survival, population aging and incidence trend. Thus it provides useful information for adequate resource management in the public health system.

The decrease in ischemic heart disease-related mortality has been one of the major factors contributing to the fall in overall mortality observed in the Italian population in the past decades[17]. This phenomenon is expected to continue in the coming years.

The absolute number of new cases tends to drop. It is realistic to hypothesize an increase in survival and consequently a decrease in mortality during the period 1990-2000. On the other hand, prevalent cases for both sexes are expected to be slightly increased in the year 2000 compared to the number of cases assessed in 1990. This is to be attributed also to the effect of population aging; as a consequence, the burden of coronary events on the public health system is expected to remain heavy.

The age-adjusted prevalence rates decreased from 1990 to the year 2000 in both genders. This decrease was more marked in the North than in the other regions, except for the prevalence rate for men in the South and for women in central Italy which remained basically stable. This means a lower number of events in the North, but not in central and southern Italy where the effects of increasing survival, population aging and incidence trend produce opposite results. Thus, despite the decrease in prevalent rates, the impact of the disease still remains higher, especially in northern Italy.

References

1. De Angelis G, De Angelis R, Frova L, Verdecchia A. MIAMOD: a computer package to estimate chronic disease morbidity using mortality and survival data. Comput Methods Programs Biomed 1994; 44: 99-107.
2. De Angelis R, Verdecchia A. MIAMOD: user's manual. Rapporti Istisan 1995; 27: 1-21.
3. Frova L, Capocaccia R, Giampaoli S, Verdecchia A. Estimating population-based incidence and prevalence of major coronary events. J Clin Epidemiol 1997; 50: 507-15.
4. Verdecchia A, Capocaccia R, Egidi V, Golini A. A method for the estimation of chronic disease morbidity and trends from mortality data. Stat Med 1989; 8: 201-16.
5. Pollard AH. The interactions between morbidity and mortality. Journal of the Institute of Actuaries 1980; 107: 233-302.
6. Durrleman S, Simon R. Flexible regression models with cubic splines. Stat Med 1989; 8: 551-61.
7. Caselli G. Future longevity among the elderly. Health and mortality trends among elderly population: determinants and implications. In: International studies in demography. Oxford: Clarendon Press, 1995: 573-81.
8. Burgio A, Frova L. Projections de mortalité par cause de décès: extrapolation tendancielle ou modèle age-période-cohorte. Population 1995; 4-5: 1031-52.
9. Tunstall-Pedoe H, Kuulasmaa K, Amouyel P, Arveiler D, Rajakangas AM, Pajak A, for the WHO MONICA Project. Myocardial infarction and coronary deaths in the World Health Organisation MONICA Project. Registration procedures, event rates and case fatality in 38 populations from 21 countries in 4 continents. Circulation 1994; 90: 583-612.
10. Hakulinen T, Abeywickrama KH. A computer program package for relative survival analysis. Comput Programs Biomed 1985; 19: 197-207.
11. Cutler SJ, Ederer F. Maximum utilisation of the life table method in analysing survival. J Chronic Dis 1968; 8: 699-712.
12. Capocaccia R, De Angelis R, Frova L, et al. Estimation and projections of stomach cancer trends in Italy. Cancer Causes Control 1995; 6: 339-46.
13. Capocaccia R, Verdecchia A, Micheli A, Sant M, Gatta G, Berrino F. Breast cancer incidence and prevalence estimated from survival and mortality. Cancer Causes Control 1990; 1: 23-30.
14. Mariotto A, Dally LG, Micheli A, Canario F, Verdecchia A. Cancer prevalence in Italian regions with local cancer registries. Tumori 1999; 85: 400-7.
15. Micheli A, Verdecchia A, Capocaccia A. Estimated incidence and prevalence of female breast cancer in Italian regions. Tumori 1992; 78: 13-21.
16. Chambless L, Keil U, Dobson A, et al. Population versus clinical view of case fatality from acute coronary heart disease; results from the WHO MONICA Project 1985-1990. Circulation 1997; 96: 3849-59.
17. Verdecchia A, Egidi V, Golin A. Popolazione italiana, invecchiamento demografico e condizioni di salute. In: Gheddes M, ed. La salute degli italiani. Rapporto 1993. Firenze: La Nuova Italia Scientifica, 1994: 193-216.