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Surveillance of ischaemic heart disease: results from the Italian MONICA populations

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Background The major objectives are to report on coronary event mortality, incidence and attack rates and changes over time observed in the Italian MONICA populations and to assess if trends are consistent when different disease definitions are considered. An analysis of diagnostic agreement between clinical and MONICA categories is presented in the context of developing a model for estimating disease incidence in a population, based on currently available data.

Methods Data were provided by the three Italian MONICA (MONItoring trends and determinants of CArdiovascular diseases) registers. The areas of Brianza and Friuli, both located in northern Italy, completed the 10-year period of registration. Data from the MONICA Latina area, located close to Rome, were limited to the first 3 years of registration. These data are used for assessing geographical differences in rates in the mid-1980s and estimating the diagnostic agreement between International Classification of Diseases (ICD) codes and MONICA categories. Two diagnostic aggregates have been used: the standard MONICA diagnostic definition for myocardial infarction (MI), which includes non-fatal definite myocardial infarction and fatal coronary events, and the coronary event definition which includes, in addition, non-fatal possible myocardial infarctions.

Results From the mid-1980s to the mid-1990s, a considerable reduction in all-cause, cardiovascular and coronary mortality rates occurred in the monitored populations. Data from the MONICA registers confirm the accuracy of official reports of death rates and changes in Italy. Comparisons of time differences in attack and incidence rates of myocardial infarction and all coronary events indicate that the impact of the more severe manifestations of coronary heart diseases (fatal coronary event and acute MI) reduced during the period of observation, but when less severe events (minor myocardial infarction and angina pectoris) are considered, the overall impact of the disease on the population remained stable.

Conclusion Epidemiological surveillance of coronary syndromes is relevant over this time period of impressive changes in prevention and treatment. Continuing restrictions in available resources necessitate the development of simplified registration systems.

Keywords Coronary heart disease, time trends, Italy

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Introduction

In Italy, mortality rates for coronary heart disease (CHD) decreased from the second half of the 1970s and during the 1980s,[1,2] heterogeneously across the whole country, with more pronounced reductions in the northern regions,[3,4] where rates were originally higher. The MONICA Project aims to understand the reasons for the decline, to determine if it is due to

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reduced incidence or to decreased case fatality (which respectively attribute the decrease in mortality to the effect of primary prevention interventions, or to more timely and effective treatment of acute events). Furthermore, from a public health perspective, recommendations may emerge for allocation of available resources.

Overall results from the WHO MONICA Project[5] indicate that two-thirds of the decline in CHD deaths may be attributed to decreases in coronary event attack rates, and one-third to decreasing trends in case-fatality. These results are inconsistent with previously published reports from the US,[6] which suggested that the decline in CHD mortality is largely due to improvements in survival of myocardial infarction cases, while first MI hospital admissions increased slightly.

Indicators of CHD occurrence based on reliable data, consistent over time, are essential, but it is very costly to maintain surveillance registers such as MONICA. Consequently, it is necessary to develop reliable registration systems, capable of being used at regional and national levels, based on currently available data:[7,8] death certificates and hospital discharge records. However, these records are rarely reliable because they are affected by different sources of variability, e.g. current medical knowledge, changes in diagnostic procedures, completeness of notification and, not least, changes in rules for reimbursement by health insurance schemes. The temporal trends in disease rates could be biased by these sources of variability.

The objectives of this paper are to report on coronary event mortality, incidence and attack rates and changes over time observed in the Italian MONICA populations and to assess if trends are consistent when different disease definitions are considered. In addition, an analysis of diagnostic agreement between current clinical and MONICA categories is presented in the context of developing a model for estimating disease incidence in a population, based on currently available data.

Methods

Monica registers in Italy

Data come from the three MONICA myocardial infarction registers set up in Italy in the mid-1980s: the areas of Brianza (1985) and Friuli (1984), located in the northern part of the country, and Latina (1983), located close to Rome. The first two registers completed the 10-year observation period, but in Latina registration activities were interrupted, due to financial constraints, after only 3 years (1983–1985). Denominators of rates come from intercensus estimates in Brianza, and from direct counts provided by municipalities in Friuli and Latina.

The MONICA myocardial infarction register has been described in detail.[9,10] Essentially it is based on a standardized system of notification and validation of suspected fatal and non-fatal coronary events. The procedures implemented in all Italian registers for notifying the events involve the systematic collection of death certificates, the selection of the relevant codes (International Classification of Diseases, Ninth Revision [ICD-9] 410–414 and other codes) and the review of hospital discharge diagnoses (ICD-9 codes 410–414). Completeness of data for fatal events was assured through a systematic collection of death certificates provided by local health units cross-checked with lists of deaths provided by municipalities. Deaths which occurred out of the municipality of residence were requested directly from the municipality where they occurred.

For hospitalized events, data collection included a systematic review of discharge diagnoses from cardiology units, coronary care units and departments of medicine of all hospitals within the register areas, as well as of neighbouring hospitals, where residents had been treated.

The MONICA myocardial infarction diagnostic criteria have been applied according to the international protocol. Diagnostic categories are based on collection of standardized information on: past history of myocardial infarction and ischaemic heart disease; symptoms at onset; maximum levels of serum enzymes; relevant electrocardiograms (coded according to the Minnesota Code and capable of describing the evolution of the lesion according to a standardized algorithm); and for fatal cases, necropsy findings. Fatal cases were classified according to the MONICA diagnostic categories: definite myocardial infarction (F1), possible myocardial infarction (F2), non-myocardial infarction (F4) and cardiovascular deaths with insufficient data (F9). Non-fatal events were classified according to three main diagnostic categories: definite myocardial infarction (NF1), possible myocardial infarction (NF2) (angina pectoris and other minor coronary syndromes) and non-myocardial infarction (NF4).

Two separate diagnostic aggregates have been used for the present report: myocardial infarction (MI) and coronary events (CE). Both of them include fatal coronary events (FCE), derived from the sum of F1, F2 and F9. This aggregate for fatal events corresponds to the MONICA validated coronary deaths. In addition, the standard MONICA diagnostic definition[5] for myocardial infarction (MI) includes non-fatal definite myocardial infarction (NF1), while the more comprehensive coronary event (CE) definition also includes possible non-fatal myocardial infarctions (NF2). Both attack rates, which include first events and recurrences, and incidence rates, which include only the first events, were calculated. The 28-day case-fatality rates were calculated as the ratios between fatal events and the total number of events, fatal or non-fatal, for both diagnostic aggregates (MI and CE). Case-fatality rates were calculated for attack events only.

Mortality, attack rate and incidence rates, for the age group 35–64 years, were standardized by the direct method, using as weights the world standard population proportions per decade of age. Case-fatality rates were weighted using the gender-specific proportions of myocardial infarctions registered in all MONICA centres.[10] Standard errors of standardized rates and of differences of standardized rates were calculated assuming the normal distributions of errors.[11]

Results

Mortality rates and time changes

Table 1 reports gender-specific mortality rates (age range 35–64 years), registered in the initial and final years of the registration period of the two northern Italian MONICA populations and temporal changes in terms of differences between them. All-cause mortality rates show statistically significant changes in rates in both populations and in both gender groups (relative decreases of 23% in Brianza, both for men and women, and 32% for men and 27% for women in Friuli). Such reductions are attributable to decreases in cancer deaths as well as in

Table 1 Age-standardized mortality rates and rate-differences (RD) over time (per 100 000). MONICA Brianza (BRI) and Friuli (FRI) residents, 35–64 years old

	Calendar years				Rate difference	95% CI	
	1984	1985	1993	1994			
All causes							
BRI-men		687.3		529.0	–158.3	–214.2	–102.4
BRI-women		312.4		239.8	–72.6	–106.5	–38.7
FRI-men	852.9		579.3		–273.6	–326.7	–220.5
FRI-women	353.9		257.4		–96.5	–130.3	–62.7
Cancer (ICD-9 140–239)							
BRI-men		313.4		244.3	–69.1	–104.2	–34.0
BRI-women		164.2		148.8	–15.4	–40.9	10.1
FRI-men	327.6		266.0		–61.6	–95.5	–27.7
FRI-women	150.4		140.0		–10.4	–33.8	13.0
Lung cancer (ICD-9 162)							
BRI-men		101.9		75.8	–26.1	–45.9	–6.3
BRI-women		10.6		11.7	1.1	–5.7	7.9
FRI-men	108.9		82.9		–26.0	–45.2	–6.8
FRI-women	12.7		15.1		2.4	–4.7	9.5
Cardiovascular disease (ICD-9 390–459)							
BRI-men		214.5		145.7	–68.8	–97.1	–40.5
BRI-women		83.1		40.3	–42.8	–58.8	–26.8
FRI-men	252.0		142.3		–109.7	–137.4	–82.0
FRI-women	90.4		55.1		–35.3	–51.5	–19.1
Ischaemic heart disease (ICD-9 410–414)							
BRI-men		122.6		89.0	–33.6	–55.3	–11.9
BRI-women		25.2		10.1	–15.1	–23.6	–6.6
FRI-men	117.8		71.8		–46.0	–65.1	–26.9
FRI-women	30.8		18.4		–12.4	–21.6	–3.2
Cerebrovascular disease (ICD-9 430–439)							
BRI-men		48.0		22.7	–25.3	–37.8	–12.8
BRI-women		32.3		13.4	–18.9	–28.6	–9.2
FRI-men	61.4		25.4		–36.0	–49.1	–22.9
FRI-women	29.9		20.5		–9.4	–19.0	0.2

cardiovascular disease mortality rates, although levels differed in men and women. In men, cancer death rates decreased in the period under observation by about 20%, mostly due to a concurrent decrease in lung cancer rates. Among women, the decrease in cancer mortality was smaller. Death rates for all cardiovascular diseases decreased markedly, by 30–40% among men and 40–50% among women, in both populations. Both changes were statistically significant. In this age range, the observed reductions in all-cause death rates are therefore attributable mainly to the decreases in cardiovascular rates in women and equally to cancer and cardiovascular mortality rates in men.

Both coronary and stroke mortality rates decreased during the observation period. Coronary death rates decreased by 28% and 39% among men in Brianza and in Friuli, respectively. The corresponding decreases for women were 60% and 40%. All changes in coronary death rates were statistically significant. Death rates due to stroke showed consistent decrements in both gender groups for both areas, ranging from 40% to 50%. The notable exception was in Friuli where there was a small and statistically non-significant decrement (–9.4%) for women.

Trends in myocardial infarction and coronary disease attack and incidence rates

Table 2 reports the 35–64 year age-standardized attack rates of coronary events for the three Italian MONICA areas at the beginning of the observation period for myocardial infarctions and coronary events. In men attack rates were higher in Brianza when compared with the other two areas: in the first half of the 1980s, men in Brianza showed an excess in MI rates of 14% and in CE rates of 24%. Women showed MI attack rates one-sixth of those registered in men, without any relevant differences across the populations. The CE attack rates were higher in Friuli.

Figure 1 shows average annual rates for the initial and final 2 years of the registration period, and the differences between the two, for both gender groups and for the MONICA registers which completed the observation period (Brianza and Friuli). Relevant decreases have been reported for validated coronary

Table 2 Age-standardized mean attack rates of coronary heart disease in the first 3-year period of MONICA Italian registers. MONICA Area Brianza, Friuli and Latina residents, 35–64 years old

			Men		Women	
		Period	Mean rates	DTr%[a]	Mean rates	DTr%[a]
Myocardial infarction[b]	Latina	1983–1985	267.9	–	48.3	–
	Friuli	1984–1986	267.9	0.0	49.4	2.3
	Brianza	1985–1987	306.1	14.3	48.1	–0.3
Coronary event[c]	Latina	1983–1985	339.4	–	75.2	–
	Friuli	1984–1986	373.8	10.1	89.8	19.4
	Brianza	1985–1987	422.4	24.4	77.5	3.1

[a] DTr% = Relative rates difference, with Latina rates as references.

[b] Myocardial infarction: MONICA diagnostic categories F1, F2, F9 and NF1.

[c] Coronary Event: MONICA diagnostic categories: F1, F2, F9, NF1 and NF2.

death rates in both gender groups and in both populations. These trends confirm the figures given by official mortality statistics.

During the decade under investigation, MI attack rates have shown a reduction in both gender groups, particularly in Brianza, where rates were higher in the initial years. In this area, a decrease of 18.5% has been observed in men and 24.7% in women. Such decreases provide an explanation for the reduction of validated coronary mortality rates of 75% for men and 50% for women. The 28-day case-fatality of MI declined in all gender- and area-specific groups, but the change was statistically significant only in Brianza women. Fatality trends seem to explain most of the decrease in coronary mortality rates in women. Statistically significant differences were observed in MI incidence rates (first events only) in men but not in women. Consistent decreases in MI case-fatality rates have been observed, although higher among women in both areas. Time changes in CE are different from the trends in MI; small decreases are detectable for attack rates in men only in both populations. The CE incidence rates show trends that are stable or slightly increasing (e.g. women in Friuli). The still statistically significant decrement in CE incident rates in the male population of Friuli is a notable exception.

Diagnostic agreement between clinical and MONICA categories

Tables 3a and 3b show the analysis of diagnostic agreement between selected ICD-9 codes and MONICA diagnostic aggregated categories, for fatal and non-fatal events respectively. The data have been provided by the three Italian MONICA registers and used all the events recorded over their entire observation period. The ICD-9 codes were identified as possible sources of myocardial infarction.

Table 3a reports the underlying causes of death reported on death certificates, coded according to the ICD rules and the validated MONICA diagnostic categories. Reported aggregations of ICD-9 codes were obtained through a sensitivity analysis, finalized to pool single ICD codes into ICD groups capable of generating the same proportion of MONICA events. For each ICD group the positive predictive value (PPV) is given, keeping the MONICA validated FCE as a reference. Very high levels of diagnostic agreement was found among fatal events for ICD codes 410–411 (96%), followed by codes 412–414 (88%) and then for codes of hypertension (401–405; 88%) and diabetes mellitus (250; 70%). The PPV for minor ICD codes (i.e. 425 and

Table 3 Analysis of diagnostic agreement between official cause of death codes and MONICA diagnostic aggregated category. Registered events in Italian MONICA centres over the entire observation period

	MONICA FCE[b]		Total	
ICD-9[a]	n	ppv[f]	n	Prevalence
a. Fatal events				
250[e]	76	0.70	109	0.012
401–405[e]	290	0.84	345	0.037
410–411	3772	0.96	3942	0.418
412–414	1015	0.88	1147	0.122
424[e]	56	0.65	86	0.009
425[e]	64	0.3	204	0.022
427[e]	461	0.61	761	0.081
428[e]	392	0.68	579	0.061
429[e]	315	0.74	424	0.045
420–423, 426[e]	20	0.57	35	0.004
440	110	0.75	147	0.016
441	39	0.42	92	0.010
442–449	49	0.56	88	0.018
798	23	0.46	50	0.010
799	187	0.53	352	0.071
Other[e]	267	0.25	1063	0.216
Total		7136	9424	

	MONICA MI[d]		Total	
ICD-9[c]	n	ppv[f]	n	Prevalence
b. Non-fatal events				
410	6605	0.82	8025	0.368
411	64	0.15	430	0.020
412	69	0.10	690	0.032
413	390	0.05	7379	0.338
414	362	0.09	3894	0.179
420–429[e]	29	0.05	554	0.025
Other[e]	53	0.06	831	0.038
Total		7572	21 803	

[a] Underlying cause of death codes.

[b] Fatal coronary event (MONICA diagnostic categories F1, F2, F9).

[c] First discharge diagnoses.

[d] Myocardial infarction (MONICA diagnostic categories F1, F2, F9, NF1).

[e] With 410–414 codes in other causes of death or discharge diagnoses.

[f] positive predicted value.

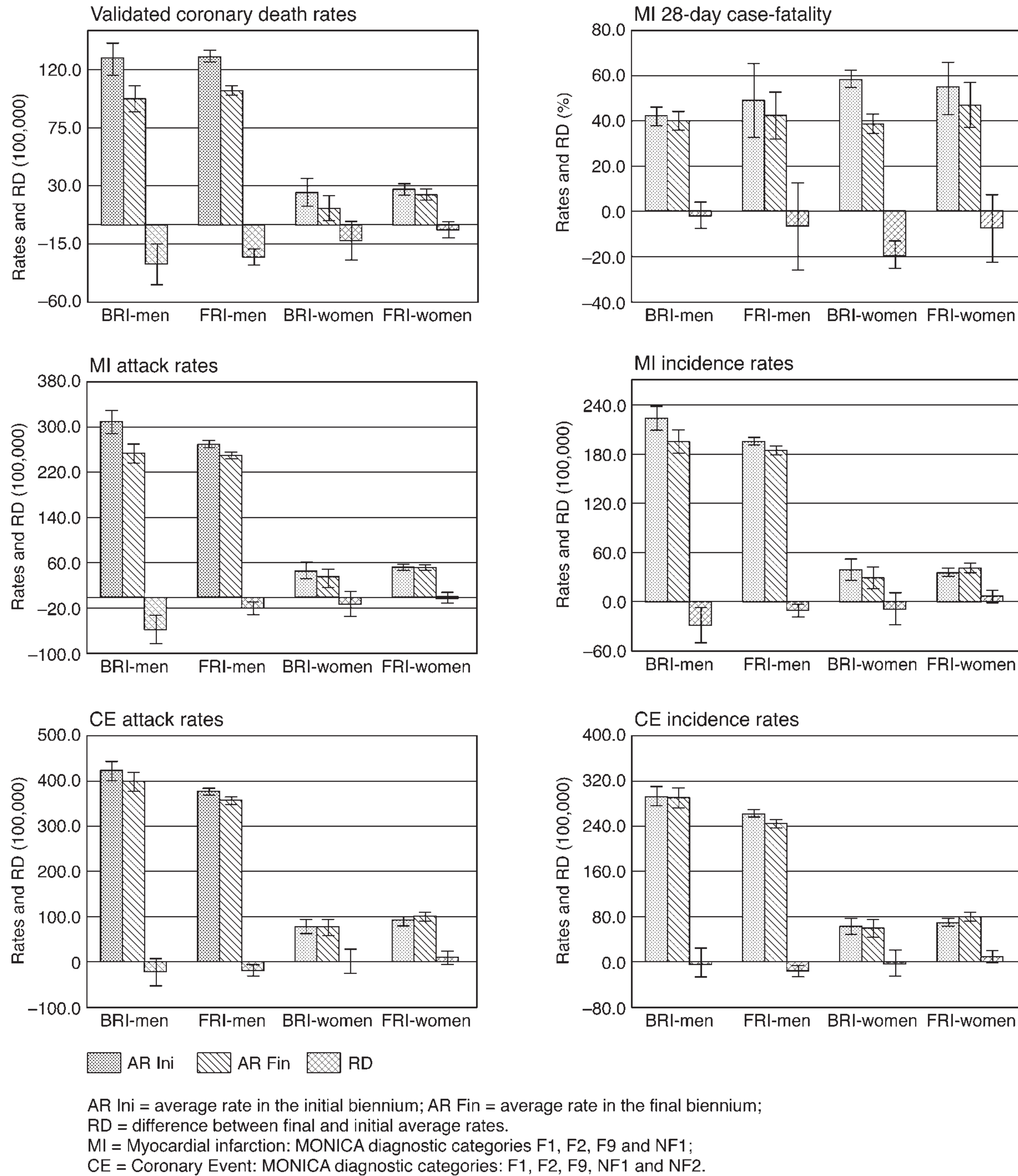

Figure 1 Age-adjusted rates and rate difference (DR) of coronary event in the Italian MONICA centres, 35–64 years old

others) range from 25% to 30%, indicating a considerable potential for generating MONICA validated FCE.

Table 3b reports the results of the analysis of the diagnostic agreement between ICD-9 codes from main diagnoses of hospital discharges and MONICA diagnostic categories for non-fatal events, using data from the three Italian MONICA registers. For the purpose of this analysis, only the MONICA diagnostic category of definite myocardial infarction (NF1) is considered as positive for myocardial infarction. Very different PPV were found for the considered ICD codes, ranging from 82% for code 410 (acute myocardial infarction) to 5% for codes 413 (angina pectoris).

Discussion

In summary, these overall Italian MONICA results indicate that from the mid-1980s to the mid-1990s coronary mortality rates continued to decrease[1,2,4] and the CHD epidemic (fatal coronary event and acute MI) in northern Italy has declined over the observation period.[5] These results also indicate that the

impact of the more severe manifestations of CHD (fatal coronary event and acute MI) diminished during the period of observation, but when less severe events (minor myocardial infarction and angina pectoris) are included, the overall impact of the disease on the population remained stable. Further study is required to assess if these trends are related to better identification and prevention of well-known risk factors or to greater effectiveness in treatment of acute events.

Even if death rates due to coronary disease provided by official statistics are somewhat lower than the MONICA validated diagnoses, the reported changes over time derived from the two registration procedures are similar. Unexpectedly, when considering the diagnostic agreement, a considerable number of the cases identified as positive coronary deaths from the two classifications are not the same. This apparent paradox is due to a certain amount of MONICA FCE hidden by non-coronary ICD codes, mainly due to the official classification rules (e.g. diabetes mellitus). These are balanced by more or less the same number of ICD coronary deaths which are not classified as such by MONICA, due to poorly available diagnostic criteria, including autopsy. Similarly, when considering diagnostic agreement of non-fatal events, some MONICA MI cases are found in a relatively wide range of non-MI hospital discharge diagnoses.

This reinforces the need for standardized registration procedures for coronary events which are capable of monitoring reliable trends over time. On the other hand, simplified registration systems are needed due to the continuing restrictions in available resources. In this context a simplified method, based on record linkage of hospital discharge diagnoses and death certificates, with intermittent validation of fatal and non-fatal events according to the standardized MONICA diagnostic criteria, has been proposed recently.[12] Essentially, this method uses sources of information and databases currently available in public health services, and it aims to identify the numbers of fatal and non-fatal major coronary events, taking into account the prevalence of ICD codes and the positive predicted values derived from comparisons to a standardized validation system like MONICA.

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KEY MESSAGES

- In the Italian MONICA populations, from the mid-1980s to the mid-1990s, there was a considerable reduction in all-cause, cardiovascular and coronary mortality rates.
- Data from MONICA registers support the accuracy of official death rates and changes in Italy.
- Comparisons of time differences of myocardial infarction and all coronary event rates indicate that the impact of the more severe manifestations of the disease (fatal coronary event and acute MI) on these populations reduced during the observation period, however, when less severe events (minor myocardial infarction and angina pectoris) are taken into consideration, the overall impact remained stable.
- The development of simplified registration systems is needed due to continuing restrictions in available resources.

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