 International Journal of Epidemiology 1999;**28**:211–218

Incidence of myocardial infarction in the Danish MONICA population 1982–1991

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Background	Cardiovascular mortality has been declining in Denmark over the past 20 years. Trends in incidence of myocardial infarction (MI) over the period 1982–1991 are described within the framework of the World Health Organization MONICA Project.
Methods	The DAN-MONICA heart register included all cases of MI in 25–74-year-old men and women living in 11 municipalities around Glostrup County Hospital evolving over a period of 10 years. They were identified retrospectively based mainly on relevant ICD diagnoses in death certificates and hospital discharge reports. Cases meeting WHO-MONICA criteria for definite or possible MI, recurrent as well as first-ever MI, were registered. Subsequent tracing of cases through national registers on deaths and hospitalizations by means of the patient's civil registration number ensured the completeness of the registration.
Results	A total of 6025 cases of MI occurred in the period, 4532 among men and 1493 among women. A total of 2923 men and 1047 women had a first-ever MI in the period. The age-standardized rates show a definite decline over the registration period for men and a less distinct decline for women.
Conclusions	The DAN-MONICA heart register meets the requirements for completeness and uniformity throughout the registration period. Causes and magnitude of bias are well described. Even when possible sources of bias are taken into account, the incidence of MI decreased significantly over the 10-year-period 1982–1991 by an average of 5.0% per year for men and 3.5% per year for women.

Keywords	Coronary heart disease, myocardial infarction, trends, incidence, epidemiology, WHO MONICA project
Accepted	29 September 1998

The last 25–30 years have seen a declining trend in cardiovascular mortality in many western countries. Ischaemic heart disease is, however, still one of the most frequent causes of death in industrialized countries.[1] As regards mortality due to heart disease, Denmark has been among the top third compared with other western countries. Even so, mortality due to cardiovascular disease has been falling in Denmark over the past 20 years.[2]

The MONICA study has attempted to clarify the background for the changes in cardiovascular mortality.[3] It is a multi-centre study within the framework of the World Health Organization system for monitoring incidence of myocardial infarction (MI) and stroke, levels of risk factors and patterns of therapy over a period of 10 years. The purpose of the study is to evaluate the extent to which the recorded changes in mortality are due to changes in incidence or lethality and the extent to which they may be explained by changes in levels of risk factors and improved treatment.

The first MONICA-centres began work in the early 1980s. The study eventually included a total of 38 well-defined populations in 21 different countries,[4] where the incidence of coronary heart disease and lethality measured in accordance with standardized diagnostic criteria differ significantly.[5–11] The Danish centre (DAN-MONICA) has participated since 1982.

The objective of the present article is to describe trends in incidence of MI in Denmark over the period 1982–1991. Methodological problems will be discussed regarding registration bias, definition of MI, and various measures of incidence.

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Material and Methods

Study population

The study population consisted of all individuals aged 25–74 living in 11 municipalities around Glostrup County Hospital in the western suburbs of Copenhagen. The average size of the population was 202 000 individuals (range 199 600–206 200).[12,13] Also the average age within each 5-year age group changed by only 0.3 years over the 10-year period for both men and women. In the following, only the age group 30–74 is included because very few cases of MI (29 or 0.2%) were found in the age group 25–29.

In addition to the age groups covered by the WHO 'core study', DAN-MONICA included the age group 65–74, since in Denmark there is no policy of restricting certain treatments to people aged less than 65, and because diagnosis according to the criteria adopted for the MONICA projects was assumed to be possible for this age group as well.

Sources and data collection procedures

The DAN-MONICA register included all cases of MI occurring in the study population over a period of 10 years.

Sources

All cases of possible heart attack occurring in the study population were identified retrospectively (cold pursuit) based mainly on relevant ICD diagnoses on death certificates and hospital discharge reports and to some extent on reports from general practitioners and nursing homes. Cases were identified as follows:

1. Non-fatal cases leading to hospitalization at the county hospitals. Records were retrieved from the archives based on a preliminary search of hospital register data. The DAN-MONICA search codes for hospital discharge diagnoses of non-fatal cases were the ICD-8 codes: acute MI 410 and suspected cardiac arrests 427.24, 427.27, 427.91, 427.97.

2. Fatal cases. Death certificates were collected directly from the local medical officers of health before being passed on to the National Board of Health. Death certificates with the following ICD-8 diagnoses as primary or contributory cause of death were processed: hypertensive heart disease 401–405, ischaemic heart disease 410–414, other heart conditions 420–429, arteriosclerosis 440–447, pulmonary embolism 450, chest pain 784, sudden unexpected death 795–796, diabetes mellitus 250, obesity 272, hypercholesterolaemia 277. The overall result was checked by extracting all cases diagnosed as acute MI from the National Cause of Death Register.

3. Non-hospitalized non-fatal cases. These events were identified from records of general practitioners and nursing homes in the area. In two periods of time—at the beginning and middle of the registration—co-operation with the general practitioners was intensified to evaluate the frequency of episodes of suspected MI in which the patient was not admitted to hospital.

4. Non-fatal cases hospitalized at hospitals outside the area. These cases were identified from the Danish National Patient Register using the same diagnostic search fields as for patients hospitalized at hospitals in the county. Commentaries and post-mortem data, if any, were collected from the hospitals in question.

For all potential cases information was retrieved from current or previous records, discharge cards, emergency ward reports, death certificates, inquest or autopsy reports. The material was processed and coded by doctors attached to the DAN-MONICA register.

Definitions and diagnostic criteria

Cases meeting the WHO criteria[14] for definite or possible MI or, if fatal, the criteria for coronary death, were included in the register. The criteria were based on symptoms, enzyme changes, ECG changes and post-mortem findings unambiguously defined in the coding instructions.

The register included cases of recurrent MI as well as those of first-ever MI, with the duration of an event defined as 28 days. Deterioration of symptoms or signs of new occlusion within this period calculated from the attack date were not regarded as a new event. Likewise fatal cases are defined as cases where death occurred within 28 days of the onset of an event.

Definition of MI

In this article the numerator for rates is defined as the sum of definite cases alive after 28 days and definite and possible cases where death occurred within 28 days.

Primary and secondary MI

A case was considered to be a recurrent event if the record entries, death certificate, or other primary data sources contained information on a previous MI. The DAN-MONICA register itself provides the possibility of identification of secondary cases in patients with several episodes over the period 1982–1991. This possibility, however, presents the risk of systematic bias when evaluating changes in incidence over time, because the possibility that a previous MI is included in the register increases over the period. Data on previous events included in the register were therefore not used when distinguishing first-ever from recurrent events.

To check the validity of the estimated trends in the rate of first-ever events, a supplementary analysis was carried out using data from the Danish National Patient Register. The DAN-MONICA register was matched with the Danish National Patient Register by means of the patient's civil registration number, and all hospitalizations with MI were identified. Since the Danish National Patient Register was not established until 1978 previous infarcts could only be evaluated over a period of 4 years for patients hospitalized in 1982. In order to obtain a uniform evaluation over the period 1982–1991, first-ever infarctions were therefore defined as cases registered in the DAN-MONICA register, where, according to the Danish National Patient Register, the patient had not been hospitalized with the diagnosis MI within the 4 years prior to the actual event. This made it possible to identify previous episodes of MI in a uniform way independently of the DAN-MONICA registration and thus avoid bias.

Quality control

The completeness of the registration was ensured by the wide search field and by subsequent tracing of cases through national registers on deaths and hospitalizations (The Cause of Death Register and the Danish National Patient Register). Patients not hospitalized were traced through general practitioners.

To evaluate false negatives all episodes of heart disease (ICD 393–429) were registered for a period of 6 months.

The validity of the diagnoses were ensured by inter- and intra-observer studies within the framework of WHO comparing the

coding of selected cases (including ECG) in the various countries. These quality control procedures were carried out throughout the entire study period at intervals of 1–2 years.

Statistics

Measure of incidence

The article presents attack rates as well as the incidence of first-ever events. The attack rate indicates the number of cases per 100 000 person-years. The same individual may be included in this calculation several times. The attack rate is a suitable measure for the load on the public health care system. The incidence is calculated as number of first-ever events per 100 000 person-years. Annual sex- and age-specific standardized rates were calculated by the direct method using the study population in 1991 as reference.

Statistical tests

The association between two categorical variables is evaluated by means of Pearson χ^2 test. To test the trend the Goodman-Kruskals γ is used. Trends in incidence are evaluated by means of Poisson regression.

Results

A total of 9638 events in the age group 30–74 years were registered, and 6025 (62.5%) met the specified criteria for MI (Table 1). In 1349 (14%) of the fatal cases data were incomplete, permitting no classification.

Changes in frequency

Attack rate

A total of 6025 cases of MI occurred in the period, 4532 among men and 1493 among women. In the age group 30–39 years the entire period had a total of 101 cases among men versus 14 cases among women and at 40–49 years there were 553 cases among men and 111 among women. Figure 1 shows the age-specific attack rate for men and women in the periods 1982–1984, 1985–1987, and 1988–1991. The curve for women has a parallel displacement of 8–10 years with increasing age when compared with men. Poisson regression revealed significant downward trends in attack rates (Table 2), which are evidence from the age-standardized rates displayed in Figure 2. Table 3 gives the attack rates in the individual age groups for the period 1988–1991.

Incidence

A total of 2923 men and 1047 women had a first-ever MI in the period. In the age group 30–39 there were a total of 80 men and 12 women who had a first-ever MI, whereas the number increased in the age group 40–49 to 425 men and 91 women. The incidence rates for the periods 1982–1984, 1985–1987, and 1988–1991 are shown in Figure 3. Here again there were statistically significant decreases in incidence over time for both sexes (Table 2 and Figure 2).

The age-standardized rates (Figure 2) show a definite decline over the registration period for men and a less distinct trend for women. Table 4 gives the incidence rates for the individual age groups in the period 1988–1991.

Table 1 Events 1982 to 1991: diagnostic category. Men and women aged 30–74

	Non-fatal events	Fatal events	N
Definite MI[a]	2922	1574	4496
Possible MI	716	1529	2245
Ischaemic cardiac arrest	101	–	101
No MI	683	764	1447
Insufficient data	–	1349	1349
N	4422	5216	9638

[a] MI = myocardial infarction.

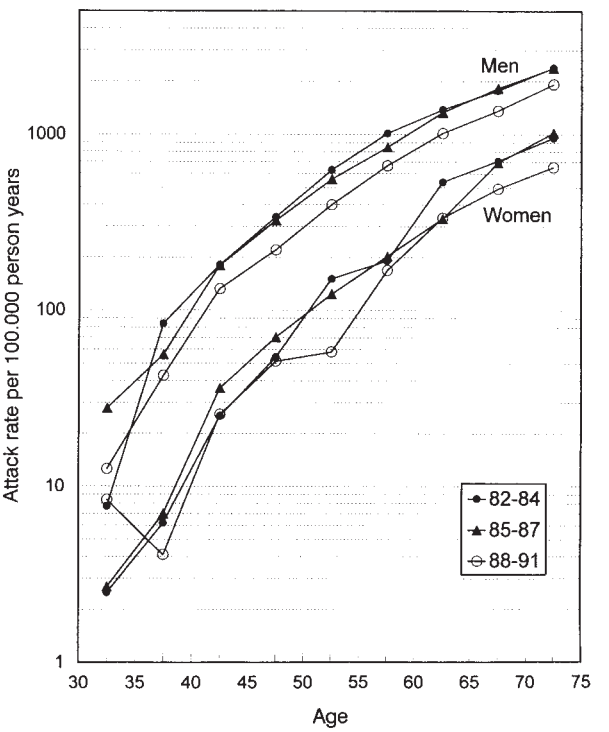

Figure 1 Myocardial infarction attack rate 1982–1991 in DAN-MONICA by age, sex and period. No. of cases per 100 000 person-years

Table 2 Estimates of time trend in attack rate and incidence rate of myocardial infarction (Poisson regression)

	Coefficient	Standard error	Decrease/year (%)	95% CI for decrease (%)
Attack rate				
Men	–0.051	0.005	5.0	4.0–5.9
Women	–0.053	0.009	5.4	3.5–7.4
Incidence rate				
Men	–0.051	0.0065	5.0	3.7–6.2
Women	–0.036	0.011	3.5	1.5–5.6

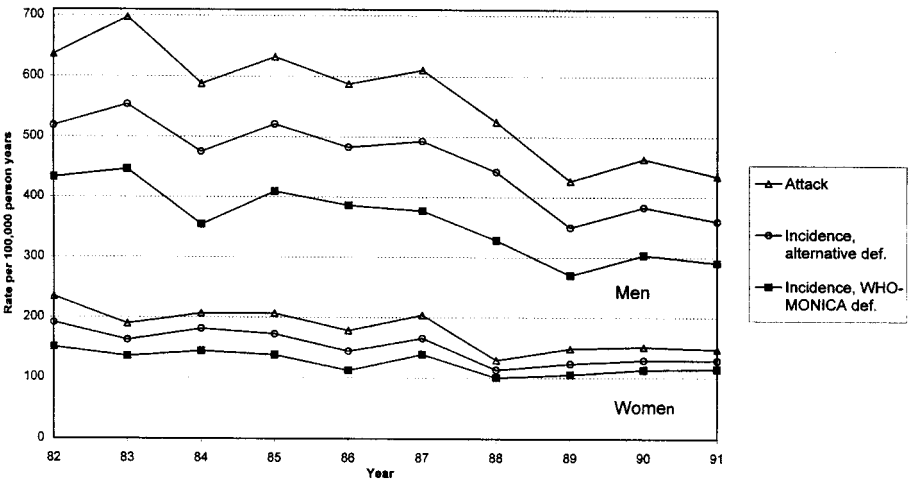

Figure 2 Age-standardized attack rate and incidence of first-ever myocardial infarction 1982–1991 in DAN-MONICA by sex using two different definitions of first-ever events

Table 3 Attack-rate of myocardial infarction 1988–1991. Men and women aged 30–74 in the DAN-MONICA population

	Men			Women		
Age	No. of events	Attacks/100 000	95% CI	No. of events	Attacks/100 000	95% CI
30–34	6	13	5–27	4	8	2–22
35–39	20	43	26–66	2	4	0–15
40–44	74	133	104–166	15	26	14–42
45–49	111	221	182–266	27	51	34–75
50–54	166	400	341–466	25	58	38–86
55–59	240	667	585–756	62	169	129–216
60–64	313	1019	909–1139	111	336	277–405
65–69	339	1364	1223–1518	139	493	414–582
70–74	319	1927	1721–2151	134	655	549–776

The validity of the observed decline in the incidence depends critically on the recording of previous events. Defining previous events on the basis of 4 years of data from the national hospital register (The Danish National Patient Register) results in overestimate of first-ever events, but ensures a high degree of uniformity throughout the period. The trend in incidence based on this alternative definition is shown in Figure 2 for comparison with the incidence based on the DAN-MONICA register alone. Although the levels are different, the curves show parallel trends in incidence. For men the incidence has gone down by 32% with both definitions and for women the decline is 24% with the DAN-MONICA definition and 33% with the alternative definition.

Quality control

Data sources

Almost all non-fatal cases (4406 out of 4422) were admitted to hospital. In 78.5% of the cases an actual record was found. Furthermore, there were additional hospital data in commentaries for a total of 99.4% of the cases. Coding was based solely on data from a general practitioner or nursing home in only 23 cases (Table 5).

Of the patients who died within 28 days, 52% had been admitted to hospital, 5% were treated by their general practitioner or at a nursing home, but 42% were medically unattended. For 11% of the cases only data from death certificates existed. There were data on record in respect of half of the cases and commentary data on two-thirds of the fatal cases. There were post-mortem data on 46.4% of the deaths (mainly among patients admitted to hospital) and further inquest reports for 9.7% (not-hospitalized).

Among the non-fatal cases data on symptoms existed in 97.5% of the cases, enzymes in 90.8% and ECG in 93.4% of the cases (Table 6).

The frequency of cases with previous MI was more or less constant both among fatal and non-fatal cases.

However, there were insufficient data in 1349 (25.9%) of the fatal cases (Table 1), of these only 52 (20%) were in the age group 30–44 years, whereas the frequency was 24–27% in the other 10-year age groups.

Insufficient data

With the chosen definition of MI an increase of fatal events with insufficient data over the 10-year period may lead to a declining trend in the number of definite and possible cases.

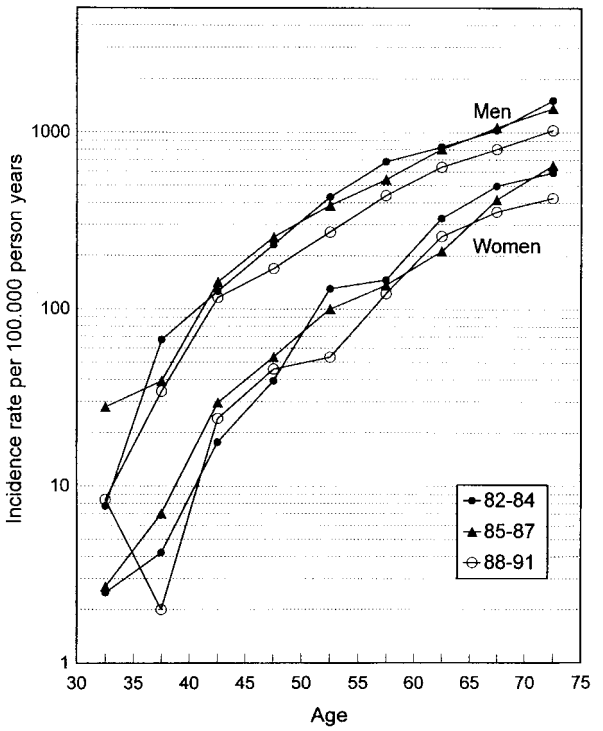

Figure 3 Myocardial infarction incidence rate 1982–1991 in DAN-MONICA by age, sex and period. No. of cases per 100 000 person-years

The average number of events with insufficient data was 117 in 1982–1985 (23.2% of coded cases), 124 (24.1%) in 1986–1988 and 170 (30.8%) in 1989–1991 (Figure 4) and hence there are 53 more fatal cases per year with insufficient data in the last period than in the first. If all these extra fatal cases with insufficient data had been definite or possible events of MI this would lead to a significant (P = 0.01) decline in the overall incidence of first-ever MI, which however is approximately only half of the observed reduction (Table 2).

For hospitalized cases the frequency of fatal cases with insufficient data was only 8.1% out of 2689 cases increasing from 7.0% in 1982–1988 to 10.5% in 1989–1991. Among non-hospitalized (fatal) cases 44.8% had insufficient data increasing from 42.6% in 1982–1988 to 48.9% in 1989–1991 (Figure 5).

The frequency of autopsy has gone down from 50.1% in 1982–1988 to 38.1% in 1989–1991. The decrease in frequency of autopsy in this period was highest among hospitalized patients (69.4%–51.3%) compared with a decline of only 2% among non-hospitalized cases. Most of these cases have hospital record information sufficient to make a MI diagnosis.

The number of death certificates from medical health officers evaluated to establish cases of MI was uneven over the period. Selection of the death certificates to be coded was based on diagnoses of clinical doctors written on the death certificates as causes of death were ICD coded in the National Board of Health afterwards. To be sure to have access to all possible death certificates with a cardiovascular cause of death we coded all death certificates with scarce or doubtful information. This resulted in

Table 4 Incidence of myocardial infarction 1988–1991. Men and women aged 30–74 in the DAN-MONICA population

	Men			Women		
Age	No. of patients	Incidence/100 000	95%CI	No. of patients	Incidence/100 000	95%CI
30–34	4	8	2–22	4	8	2–22
35–39	16	34	20–56	1	2	0–11
40–44	66	118	91–150	14	24	13–40
45–49	85	169	135–209	25	48	31–70
50–54	115	277	229–333	24	56	36–83
55–59	159	442	376–516	47	128	94–170
60–64	200	651	564–748	86	261	208–322
65–69	204	821	712–942	101	358	292–435
70–74	177	1069	918–1239	90	440	354–541

Table 5 Sources of information in 4422 non-fatal and 5216 fatal events

	Non-fatal events		Fatal events		MI[a]-cases according to WHO	
	N	%	N	%	N	%
Hospital record	3472	78.5	2584	49.5	4123	68.4
Discharge letter	4395	99.4	3516	67.4	5366	89.0
GP/Nursehome	23	0.5	35	0.7	31	0.5
Former hospital record	1459	33.0	890	17.1	1423	23.6
Medico legal			505	9.7	160	2.6
Autopsy			2420	46.4	1897	31.4
Death certificate			5132	98.4	3052	50.6
Other	5	0.1	52	1.0	26	0.4
Total	4422	100	5216	100	6025	100

[a] MI = myocardial infarction.

Table 6 Diagnostic sources. Frequency of available information about symptoms, enzymes and ECG

	Non-fatal events		Fatal events		MI[a]-cases according to WHO	
	N	%	N	%	N	%
Symptoms	4310	97.5	2703	51.8	4875	80.8
Enzymes	4015	90.8	847	16.2	3550	58.8
ECG	4129	93.4	1193	22.9	3885	64.4
Total	4422	100	5216	100	6032	100

[a] MI = myocardial infarction.

Table 7 For hospitalized cases only: frequency of how often 'former MI [myocardial infarction] = yes' was noted in cases with and without autopsy

	Autopsy performed		Autopsy not performed	
	Former MI	%	Former MI	%
1982–1988	579	43.9	152	26.1
1989–1991	121	30.0	89	23.2
N	700		241	
P-values	$P < 0.0001$		$P = 0.30$	

a fluctuating and high number of rejected (no-MI) cases and in many non-hospitalized fatal cases with insufficient data. Per year the average number of cases coded on basis of death certificates alone was 45 in 1982–1985, 62 in 1986–1988 and 67 in 1989–1991. This increase is not statistically significant ($P > 0.3$). A similar change seems to have occurred among our coders in their tendency to interpret a case with scanty information as insufficiently reported.

Discussion

Using WHO-MONICA criteria and definitions a total of 6025 cases of MI living in a well-defined geographical area in the period 1982–1991 and having age 30–74 were identified, 3970 of these being first-ever events. Both attack rate and incidence of first-ever MI declined significantly over the 10-year-period, the first-ever incidence by 5.0% per year for men (95% CI : 4.0–5.9) and 3.5% per year for women (95% CI : 1.5–5.6). A marked increase in the frequency of fatal cases with insufficient data and decrease in the frequnecy of autopsy was seen.

Data quality

For secular trends based on a register to be valid, that register must be *complete*. It is unlikely that the DAN-MONICA register omitted many cases of MI in its study population. The incidence of suspected non-hospitalized MI was evaluated in two periods at the beginning and middle of the registration through intensive contact with general practitioners. The incidence was less than 1% in each of the two periods. In a period where an extended search field was applied, 1% cases with definite or possible MI were found per year. The number of 'false negative cases', i.e. patients being hospitalized or dying with other diagnoses than those leading to coding by means of the search field of DAN-MONICA, must therefore be considered to be negligible. 'False definite cases', i.e. patients included in the search field due to suspected MI, which could later be disproved on the basis of MONICA criteria, were of the same order as in the majority of the MONICA centres.[14]

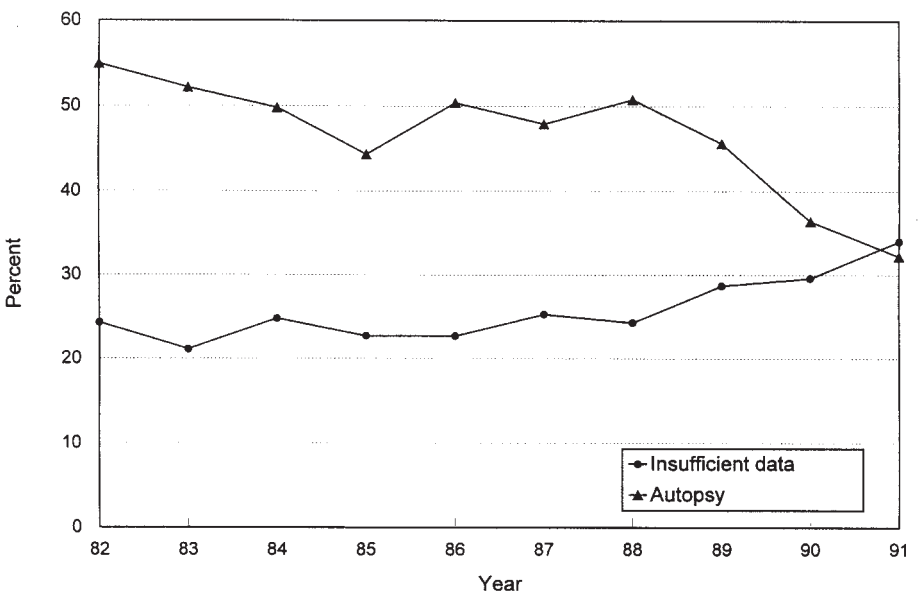

Figure 4 Frequency of cases with insufficient data compared to the frequency of autopsy 1982–1991

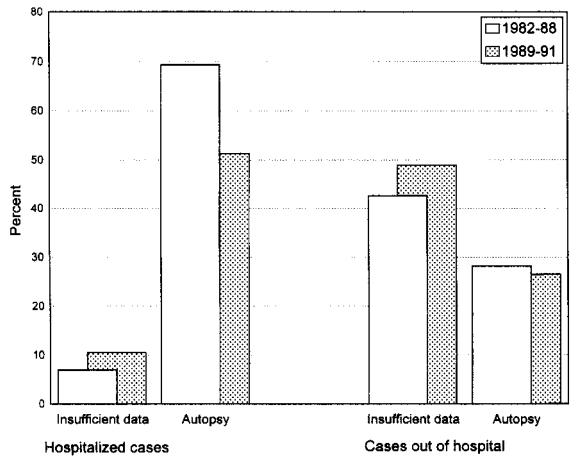

Figure 5 Frequency of cases with insufficient data and autopsy 1982–1988 compared to 1989–1991 according to hospitalization

Thrombolytic therapy of the acute attack has become more and more routine since 1987. That year 2.4% had streptokinase, later this was used in approximately every fifth case. In principle, the introduction of thrombolytic therapy should not affect the incidence, but it may have affected the possibility of establishing the diagnosis. As the treatment is being implemented very soon after admission to hospital it may sometimes have the effect of precluding the usual enzyme increase which may again diminish the infarct to below detection limit. Consequently, the infarct does not meet the WHO diagnostic criteria.

The registration ought to be *uniform* throughout the period. Five doctors performed the coding of records as regards MI in the period. The inter-coder variation was checked on a regular basis and this was of the same magnitude as the intra-coder variation and did not increase over time. The tendency to interpret cases with scanty information as cases with insufficient data seems to have contributed to an increase in fatal cases with insufficient data.

A few aspects of the MONICA manual have been changed over the period but as these changes concern further specification rather than change of data they should not have significantly influenced the uniformity and use of the register.

Insufficient data

Compared with other centres DAN-MONICA does not differ[14] regarding hospitalization frequency for non-fatal cases or the degree of information on symptoms, enzymes and ECG. The incidence of fatal cases with insufficient data is a little above average compared with other centres even though far more patients were hospitalized. The reason may be that the distances in Denmark are so short that many very ill patients reach the hospital alive but do not live long enough to allow complete investigations. The older age groups included in the study may lead to a higher frequency of insufficient cases as insufficient cases are more common among the elderly.

A legislative amendment introduced in 1990 requiring permission from relatives before performing an autopsy has reduced significantly the frequency of post-mortem, in particular among hospitalized cases, where it decreased by 25%. This trend began, however, some time before the amendment became effective and explains to some extent the increase in the number of cases with insufficient data. Still, the impact of this is rather limited as other diagnostic alternatives are available as regards patients admitted to hospital.

It is a central purpose of MONICA to monitor the trend in sudden death, as such deaths could introduce an artefact into apparent trends in deaths from heart disease. In Denmark the interpretation of the official cause of death statistics has been difficult due to an increased incidence in deaths from unknown causes (ICD 795) in all age groups from the 1960s until now, and a simultaneous reduction in mortality due to ischaemic heart disease.[15] As we have evaluated such deaths according to standardized criteria of WHO we should have eliminated this source of error.

Trends in incidence

A valid evaluation of trends in incidence requires a uniform registration of cases of MI over the period and a definite and uniform identification of first-ever events.

Our data show a decline in incidence throughout the entire period. The particularly significant decrease over the last few years may to some degree be attributable to the introduction of thrombolytic therapy, which not only reduces case fatality[16] but also the extent of the infarct—even to below the detection limit.[17,18] The increase in the number of cases with insufficient data has some impact on first-ever incidence of MI. If the additional cases with insufficient data recorded in 1989–1991 were considered definite or possible MI this would approximately half the decrease in incidence—however it would still be significant.

The coded incidence of cases with previous MI is higher in the group on which post-mortem has been performed. As the frequency of post-mortem went down over the last 3-year period, a reduction in the proportion of cases with previous infarct was to be expected. This was not the case, however. Theoretically, a reduced possibility to detect previous MI by means of post-mortem might lead to an overestimation of first-ever events in the last period and thereby an underestimation of the actual decrease in incidence. A slight underestimation of the number of first-ever events in the first registration period was probably the case, as previous MI was coded from hospital records stating previous hospitalizations with symptoms of ischaemia.[19] The degree of documentation of previous MI was not recorded, because the manual did not state it until after 1983. Our alternative definition of previous cases based on the Danish National Patient Register, will on the other hand, result in an overestimation of the first-ever events as only cases which occurred over the previous 4 years can be included. In the case of both definitions we find, however, a definite declining incidence. For men the relative reduction is identical and for women the reduction is larger if data from the National Patient Register are used.

Theoretically, shifts in the average age within each 5-year age group towards an older or younger cohort might influence the evaluation of trend in incidence. The average age, however, was constant in all 5-year age groups over the 10-year period.

The incidence of MI in women is low, and the evaluation of changes in incidence over the period is therefore more uncertain among women than men. This may contribute to the

fact that the changes in women are more ambiguous. It is also possible that the real change in incidence among women differs from that among men. In Denmark the prevalence of smoking among men has gone down quite significantly since the 1950s, but the prevalence among women increased until 1970 and has since been almost constant.[20]

Trends in the incidence of MI in Denmark have been studied earlier in a national survey based on the Danish National Patient Register and the Cause of Death Register.[2] That register-based study also demonstrated a reduction in the incidence from 1982 to 1992, but the reduction was relatively less significant than in the present report. The percentage reduction from 1982 to 1992 was 18% for men and 16% for women, as opposed to 33% for men and 24% for women in the present study.

Compared with other MONICA centres, the incidence of MI in DAN-MONICA is among the top third together with the other Scandinavian countries.[14] Other MONICA centres have conducted studies of the changes in incidence over time. In Finland similar results with declining attack rate and incidence of first-ever infarcts in men have been found, whereas the changes among women are minor and definite reductions were not seen.[9] In Australia declining attack rates of fatal cases were seen for both sexes, but non-fatal events fell only in men.[8]

Conclusion

The DAN-MONICA heart register achieved a high standard of completeness and uniformity throughout the registration period. Even when possible sources of bias are taken into account the incidence of MI fell significantly and constantly over the 10-year period 1982–1991. On average the incidence went down by 5.0% per year for men and by 3.5% per year for women.

Acknowledgement

The Danish Heart Foundation has supported register extracts, the operation of the Heart Register and computer registration in the period 1981–1992.

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