

Incidence of first acute myocardial infarction in the Netherlands

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ABSTRACT

Objectives: To study the incidence of first acute myocardial infarction (AMI) in the Netherlands.

Background: We recently showed that AMI patients can be followed longitudinally within Dutch national medical registrations in a valid way. This makes it possible to provide nationwide incidence estimates of first AMI in the Netherlands.

Methods: New cases of first AMI in the Dutch population in 2000 were identified through linkage of the national hospital discharge register, the population register and the cause of death statistics and included hospitalised first AMI patients and out-of-hospital deaths from first AMI.

Results: 31,777 patients with a first AMI were identified. The incidence (per 100,000 persons per year) increased from 2 in men aged <30 years to 2996 in men aged ≥90 years. Corresponding figures for women ranged from 1 to 2226. The incidence was higher in men than in women in all age groups, but the male-to-female ratio decreased after the age of 50-59 years. Of all first AMI patients, 40% died before being admitted to a hospital. The proportion of non-hospitalised AMI patients increased with age in men after the age of 40-49 years and in women after the age of 50-59 years. Within the age groups, the proportion of out-of-hospital deaths was similar for men and women.

Conclusion: Our study provides the first nationwide incidence estimates of first AMI in the Netherlands. Expected differences in incidence with regard to age and gender were shown. The large proportion of out-of-hospital deaths reinforces the importance of primary prevention of AMI.

KEYWORDS

Acute myocardial infarction, coronary heart disease, epidemiology, hospital admissions, incidence, medical record linkage, registries

INTRODUCTION

Cardiovascular disease and particularly acute myocardial infarction (AMI) represent a great burden of morbidity and mortality in the Netherlands,¹ as well as in many other Western countries. Information on incidence and mortality of AMI is important for developing and maintaining public health strategies in primary and secondary prevention as well as for monitoring the effects of primary and secondary prevention on incidence and mortality. Information on incidence of acute myocardial infarction tends to come from specifically developed registries, such as the MONICA registries,² cohort studies,^{3,5} and from linkage of regional registries.⁶⁻¹⁰ Only a few countries provide nationwide data on the incidence of AMI.⁶⁻¹⁰ In the Netherlands the incidence of AMI is derived from local primary care registries¹¹ and mortality and hospital discharge rates for AMI were traditionally frequently examined for the Netherlands using national registries.^{1,12,13} Yet, since it was not possible to track subjects between and within these national registries, the information was of limited value. After we recently showed that hospitalised patients in the Netherlands could be followed longitudinally within Dutch national medical registrations in a valid way,¹⁴ we set out to study the incidence of first AMI encompassing the entire country, with particular emphasis on the proportion not hospitalised.

METHODS

Sources of data

Data on hospital admissions were derived from the Dutch National Hospital Discharge Register (HDR). Since 1986, all general and university hospitals and most single speciality hospitals are participating in the HDR. There are no private hospitals in the Netherlands that treat patients with AMI. For each hospital admission a new record is created in the HDR, including the following information: date of birth, gender, the numeric part of the postal code (since 1991), hospital-specific patient identification code, type of hospital, admission date and principal diagnosis of the admission. The principal diagnosis is determined at discharge and is in retrospect the main reason for admission. The principal diagnosis is coded using the ninth revision of the International Classification of Diseases (ICD-9-CM).¹⁵ Following individuals over time based on HDR information only is difficult, as different admissions from the same person cannot be recognised adequately. The hospital-specific patient identification code can only be used if patients return to the same hospital, provided that this code is correctly applied. A combination of partial identifying variables (i.e. date of birth, gender and numeric part of postal code) can be used to identify different admissions from the same person provided this combination is unique in the population (it has been shown that 86% of the Dutch population had a unique combination of date of birth, gender and numeric part of postal code on 1 January 1996)¹⁴ and constant over time. The numeric part of postal code, however, can change when patients move (estimated rate of 6% per year).⁵ When these patients are subsequently admitted to a hospital that does not register a (usable) hospital-specific patient identification code (19% of the hospitals in 1996) or to another hospital, recognition of these admissions is impossible. Therefore to solve this issue in tracking patients we additionally used information from the Dutch Population Register (PR). This database contains information on all registered persons living in the Netherlands, including date of birth, gender, current address, postal code, nationality and native country (both of registered person and his/her parents). Patients registered in the HDR were identified in the PR using linkage variables 'date of birth', 'gender' and 'numeric part of postal code'. When patients moved, their hospital admissions were recognised by using the new postal code registered in the PR. Information on native country in the PR was used to allocate patients in origin categories. Patients whose parents were both born in the Netherlands were classified as native Dutch.

Data on numbers of deaths from AMI in the Netherlands were derived from the national cause of death statistics. These mortality data are virtually complete and comprise

both primary and secondary causes of death. Death has been coded using the tenth revision of the International Classification of Diseases¹⁶ (ICD-10).

Privacy issues

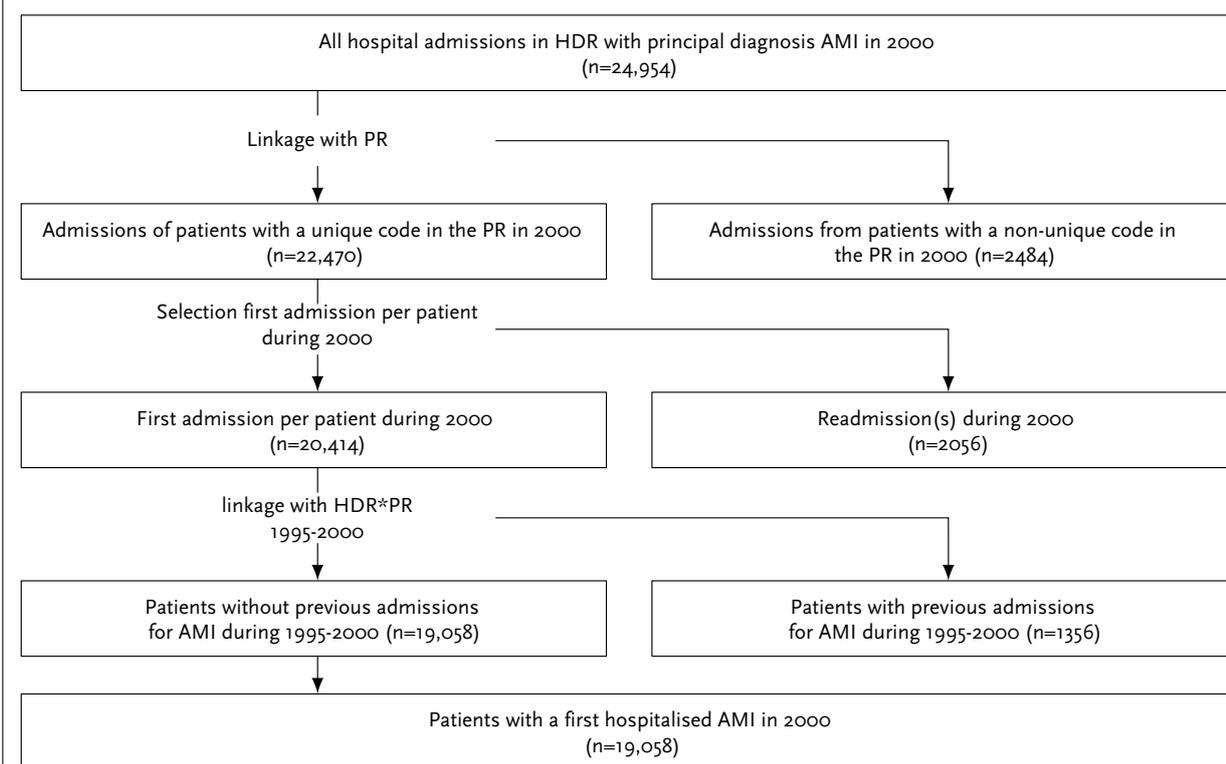
Linkage of data from the different registers was performed in agreement with the privacy legislation in the Netherlands. Anonymous follow-up was achieved by linking on the variables date of birth, gender and numeric part of postal code. After the linkages, this information was replaced in the database by less specific variables (i.e. age in years and municipal code) to further prevent identification of an individual. All linkages and analyses were performed at Statistics Netherlands in a secure environment ensuring that results meant for publication do not reveal information on individual patients, health care workers or institutions.¹⁴

Cohort enrolment

New cases of first AMI in the Dutch population in 2000 were identified through combining information of the HDR, PR and cause of death statistics and included hospitalised first AMI patients and out-of-hospital deaths from first AMI, as described in detail below.

Between 1 January and 31 December 2000, a total of 24,954 hospital admissions with principal diagnosis AMI (ICD-9-CM¹⁶ code 410 and subcategories) were registered in the HDR (*figure 1*). This included both patients hospitalised for a first AMI and patients hospitalised for a reinfarction, and both patients discharged alive and patients who died during their hospitalisation. After linkage with the PR, 22,470 admissions from patients with a unique combination of linkage variables in the PR remained in the study population (90%). Thus, each remaining admission linked to only one unique person in the PR (one unique individual in the Netherlands). Admissions linking with more than one person (e.g. administrative twins; two persons with the same date of birth, gender and numeric part of postal code registered in the PR) (7%) or with no person at all (e.g. illegal immigrants or administrative errors) (3%) in the PR were excluded. Selection of the first admission per person of all subsequent admissions of a person occurring during the year 2000 yielded a total of 20,414 patients. Accordingly, 2056 readmissions for an AMI had occurred during the year 2000 (9%). Information on hospital admissions in previous years was obtained by linking of the HDR during the period 1 January 1995 until the (first) admission for an AMI in 2000 to the PR. All uniquely linked hospital admissions with a principal diagnosis of AMI were selected and linked to the above-mentioned cohort of 20,414 patients. Patients with previous admissions for AMI were excluded (1356 patients (7%)). This resulted in the final cohort consisting of 19,058 patients with a first hospitalised AMI in the Netherlands in 2000 (*figure 1*).

Figure 1. Flowchart of the selection process of patients with a first hospitalised acute myocardial infarction (AMI) in 2000 in the Netherlands



HDR = Dutch National Hospital Discharge Register, PR = Dutch Population Register.

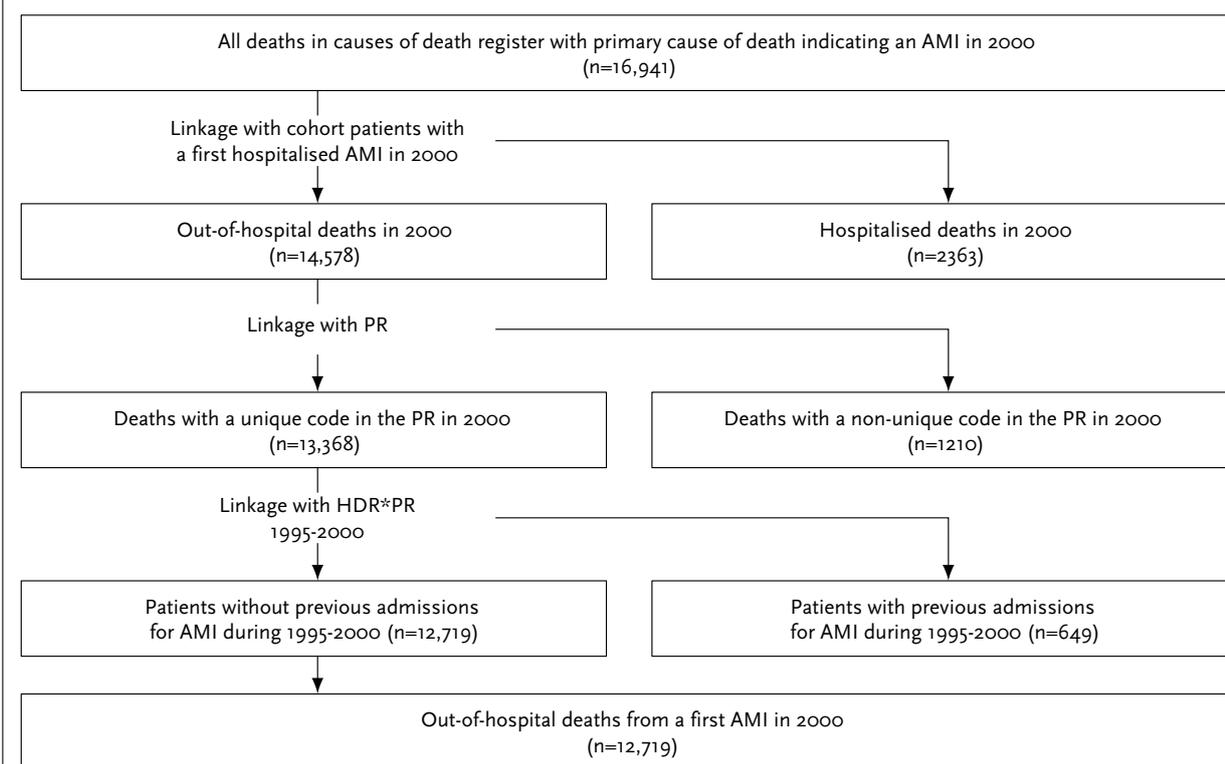
Between 1 January and 31 December 2000, a total of 16,941 deaths with as primary cause of death AMI (ICD-10⁶ code I21) or other ICD-10⁷ codes presumably indicating acute cardiac mortality (I22: subsequent myocardial infarction, I23: current complications following AMI, I24.8: other forms of acute ischaemic heart disease, I24.9: unspecified acute ischaemic heart disease, I46: cardiac arrest, R96: sudden death with unknown cause) were registered in the cause of death statistics (figure 2). This included both patients who died in hospital and those who died out of hospital. Selection of patients who were not already included in the cohort of patients with a first hospitalised AMI in 2000 (as described earlier) yielded a total of 14,578 out-of-hospital deaths. Subsequent selection of the out-of-hospital deaths with a unique combination of linkage variables 'date of birth', 'gender' and 'numeric part of postal code' in the PR, 13,368 out-of-hospital deaths remained in the study population (92%). Information on previous hospital admissions of the out-of-hospital deaths was collected analogously to the collection of information on previous hospital admissions of the patients with a first hospitalised AMI in 2000. Patients with previous admissions with a principal diagnosis of AMI during the

period 1 January 1995 until the date of death from an AMI in 2000 were excluded (649 patients (5%)). This resulted in the final cohort consisting of 12,719 out-of-hospital deaths from a first AMI in the Netherlands in 2000 (figure 2).

Data analysis

The incidence of patients with a first AMI in 2000 (with 95% confidence interval (95% CI)) was computed by age and gender. This was done by dividing age and gender-specific numbers of patients with a first AMI in 2000 with corresponding age and gender-specific numbers of unique persons in the PR at 1 July 2000. Unique persons were defined as persons who were unique in the population on the combination of values of the linkage variables. In this way, the numbers of unique persons in the PR at 1 July were used as an estimate of person-years at risk. The incidence in men was compared with the incidence in women by calculating incidence rate ratios (or relative risks) (with 95% CI) by age. The 95% confidence intervals were estimated assuming that the observed number of AMI cases followed a Poisson distribution.¹⁷ The proportion of out-of-hospital deaths of the total number of first AMI

Figure 2. Flowchart of the selection process of out-of-hospital deaths from a first acute myocardial infarction (AMI) in 2000 in the Netherlands



HDR = Dutch National Hospital Discharge Register, PR = Dutch Population Register.

patients was computed by age and gender. Within the age groups, the difference in proportion of out-of-hospital deaths between men and women was tested with the χ^2 test for homogeneity of proportions. A p value less than 0.05 was considered statistically significant.

RESULTS

In 2000, we identified 31,777 patients with a first AMI of whom 19,058 were hospitalised (60%) and 12,719 died out of hospital (40%). Two-thirds of the hospitalised patients (table 1) and 55% of the out-of-hospital deaths (table 2) were men. The patients dying out of hospital were on average 9 years older than patients dying in hospital. The age of women at admission was on average 7 to 8 years higher than that of men. The mean length of hospital stay was ten days. During admission, 12% of the patients died (men 10%, women 17%). In both the hospitalised patients and the out-of-hospital deaths, most patients were native Dutch (88-90%). AMI was the primary cause of death in 72% of the out-of-hospital deaths, cardiac arrest in 21% and sudden death with unknown cause in 6%.

Table 1. Characteristics of patients with a first hospitalised acute myocardial infarction in the Netherlands in 2000

	Men	Women	Total
Number of patients	12,783	6275	19,058
Age at admission (years):			
• Mean (SD)	64.2 (12.7)	71.6 (12.8)	66.7 (13.2)
• Median	65.0	73.8	68.0
Type of hospital (%):			
• University	7.5	6.2	7.0
• Peripheral	92.5	93.8	93.0
Length of stay (days):			
• Mean (SD)	8.9 (8.4)	10.0 (10.7)	9.2 (9.3)
• Median	7.0	8.0	8.0
• 25 th -75 th percentile	5.0-10.0	5.0-12.0	5.0-11.0
Origin (%):			
• Native	88.3	88.4	88.4
• Non-native	11.7	11.6	11.6

The incidence of a first AMI increased with age in both men and women (table 3). In men, the incidence (per 100,000 persons per year) increased from 2 (95% CI 2 to 3) in the age group younger than 30 years to 2996 (95% CI 2718 to 3274) in the age group of 90 years and older, in

Table 2. Characteristics of out-of-hospital deaths from a first acute myocardial infarction in the Netherlands in 2000

	Men	Women	Total
Number of patients	6972	5747	12,719
Age at death (years):			
• Mean (SD)	72.0 (13.2)	80.0 (11.5)	75.6 (13.1)
• Median	74.0	82.1	77.9
Origin (%):			
• Native	90.4	89.7	90.1
• Non-native	9.6	10.3	9.9
Primary cause of death (ICD-10 ⁸ code) (%):			
• Acute myocardial infarction (I21)	73.6	70.5	72.1
• Subsequent myocardial infarction (I22)	0.1	0.2	0.1
• Current complications following acute myocardial infarction (I23)	0.0	0.0	0.0
• Other forms of acute ischaemic heart disease (I24.8)	0.2	0.4	0.3
• Unspecified acute ischaemic heart disease (I24.9)	1.0	1.2	1.2
• Cardiac arrest (I46)	20.2	21.3	20.7
• Sudden death with unknown cause (R96)	4.9	6.4	5.6

women from 1 (95% CI 0.5 to 1.2) to 2226 (95% CI 2100 to 2351) in the corresponding age groups. In all age groups, the incidence of both hospitalised and non-hospitalised first AMI was higher in men than in women (table 4). This was most pronounced in the age group 50-59 years, in which the incidence was four times higher in men compared with women. After the age of 50-59 years, the male-to-female ratio decreased, indicating a relatively high increase in incidence of women older than 50-59 years.

The proportion of out-of-hospital deaths from a first AMI of the total number of first AMI patients increased with age in men after the age of 40-49 years (from 19 to 85%) and in women after the age of 50-59 years (from 21 to 82%) (figure 3). There was no statistically significant difference in proportion of out-of-hospital deaths between men and women within the age groups. In the age groups up to 70-79 years, the majority of first AMI patients were hospitalised, in the age groups 80-89 years and ≥90 years most patients died before being admitted to a hospital.

DISCUSSION

Our study provides estimates of the incidence of patients with a first AMI in the Netherlands. These estimates are based on linkage of Dutch national registries and represent for the first time virtually the whole Dutch population. An increasing incidence with age and a higher incidence in

Table 3. Incidence (per 100,000 persons per year) of first acute myocardial infarction (AMI) by age and gender in the Netherlands in 2000

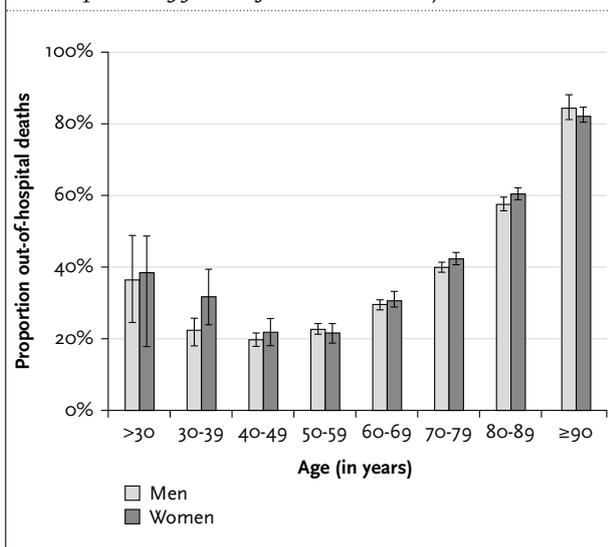
	Age (years)	Hospitalised patients	Out-of-hospital deaths	Total number of first AMI cases	Total number of persons*	Incidence	95% CI
Men	<30	37	21	58	2,576,315	2	2-3
	30-39	356	98	454	1,098,227	41	38-45
	40-49	1450	346	1796	1,011,713	178	169-186
	50-59	2960	845	3805	892,870	426	413-440
	60-69	3344	1375	4719	606,735	778	756-800
	70-79	3291	2189	5480	399,574	1371	1335-1408
	80-89	1276	1721	2997	138,020	2171	2094-2249
	≥90	69	377	446	14,886	2996	2718-3274
	All ages	12,783	6972	19,755	6,738,340	293	289-297
Women	<30	13	8	21	2,485,992	1	1-1
	30-39	90	41	131	1,067,573	12	10-14
	40-49	374	102	476	989,158	48	44-52
	50-59	692	186	878	867,587	101	95-108
	60-69	1250	550	1800	637,725	282	269-295
	70-79	2108	1536	3644	531,798	685	663-708
	80-89	1533	2326	3859	283,866	1359	1317-1402
	≥90	215	998	1213	54,502	2226	2100-2351
	All ages	6275	5747	12,022	6,918,201	174	171-177

*Number of unique persons in the PR on 1 July 2000.

Table 4. Age-specific gender ratios (RR) of the incidence of first acute myocardial infarction (AMI) in the Netherlands in 2000

Age (years)	Hospitalised first AMI patients		Out-of-hospital deaths from a first AMI		Total number of first AMI patients	
	RR Men/women	95% CI	RR Men/women	95% CI	RR Men/women	95% CI
<30	2.75	1.46-5.17	2.53	1.12-5.72	2.67	1.62-4.39
30-39	3.85	3.05-4.85	2.32	1.61-3.35	3.37	2.77-4.09
40-49	3.79	3.38-4.25	3.32	2.66-4.14	3.69	3.33-4.08
50-59	4.16	3.83-4.51	4.41	3.77-5.17	4.21	3.91-4.53
60-69	2.81	2.63-3.00	2.63	2.38-2.90	2.76	2.61-2.91
70-79	2.08	1.97-2.19	1.90	1.78-2.02	2.00	1.92-2.09
80-89	1.71	1.59-1.84	1.52	1.43-1.62	1.60	1.52-1.68
≥90	1.18	0.90-1.54	1.38	1.23-1.56	1.35	1.21-1.50

Figure 3. Proportion of out-of-hospital deaths from a first acute myocardial infarction (AMI) of total number of first AMI patients in 2000 in the Netherlands (error bars represent 95% confidence intervals)



men compared with women were shown, as well as a large proportion of out-of-hospital deaths.

Strengths of our study are the high linkage percentages obtained using this approach, the large size of the cohorts and the lack of selection bias. Recently, a high validity of both the HDR and the PR has been demonstrated. In a random sample of the HDR, 99% of the personal, admission and discharge data and 84% of the principal diagnoses (validated through medical record review by medical specialists) were correctly registered.¹⁸ This unfortunately was based on the principal diagnosis for all patients and all specialities. Therefore subjects with an AMI during hospitalisation but not coded as such may still have been missed, and patients may have been labelled as an AMI, whereas in truth this was not the case. The magnitude of both aspects cannot be estimated,

unfortunately. In a random sample of the PR, over 97% of the addresses were correctly registered and only 0.4% of days and months of birth were missing.¹⁹ Furthermore, over 97% of the uniquely linked hospital admissions resulting from linkage of the HDR with the PR were shown to be correctly linked and the estimated rate of mismatches (false-positive linkages) was approximately 1%.¹⁹

There are a number of critical aspects of our study that need consideration in order to appreciate the findings. First, the information on previous admissions was limited to a maximal five years for the patients (as the numeric part of the postal code has been registered in the hospital register since 1991). Therefore, it seems likely that some 'first' AMI patients were actually recurrent AMI patients. It has been estimated that most recurrent events (95%) occur within five years,^{20,21} which means that our incidence rates reflect a 5% overestimate of first-ever AMI. Secondly, the cause of death information used in our study was not validated by medical records or autopsy reports. It is known that the quality of routine mortality statistics varies over time and between countries. Several studies published in the 1980s have shown that the validity of the Dutch national cause of death statistics was higher than the average validity of eight countries of the European Community.^{22,23} More recent studies estimating the degree of misclassification of coronary heart disease are, however, not available. As a consequence, the degree of misclassification in our estimates of the incidence of non-hospitalised first AMI in the Netherlands is unquantifiable, but, as in almost every study using data from vital statistics, some degree of misclassification is inevitable, especially in the very old in whom only limited diagnostic effort is made. Thirdly, when we restrict our out-of-hospital deaths to AMI only, the overall incidence of out-of-hospital death will be reduced by 27%, reducing the overall out-of-hospital death considerably to 28% in men and 39% in women. Fourthly, we assumed that AMI is such a severe and alarming disease that you either die of or are treated in hospital. Therefore, most diagnosed

cases of AMI in a population can be identified through combining information on hospital admissions and deaths from national registries as done in our study. Non-fatal and non-hospitalised AMIs were lacking in our estimates. However, unpublished data from the Rotterdam Study,²⁴ a population-based cohort study among 7983 men and women aged 55 years and over showed that 1.7% of all non-fatal AMIs were not hospitalised (personal communication Dr J.C.M. Witteman). Although the Rotterdam Study included data obtained from residential care homes, no information was obtained from nursing homes. Therefore the 1.7% might be an underestimation. Yet, less than 1% of the Dutch population was admitted to a nursing home in 2000²⁵ and one may also question the correctness of the diagnosis in those subjects. Unnoticed or silent AMIs were not included in our study, in line with other record linkage studies.²⁶ If we had included silent AMIs, this probably would have yielded much higher estimates, as De Bruyne *et al.*²⁷ demonstrated that the prevalence of silent AMI was only slightly smaller than the prevalence of symptomatic AMI (4.1 and 3.9%) in persons aged 55 years or older. Fifthly, another aspect that needs to be addressed is the small percentage of subjects of the cohort that could not be traced back completely in the period 1995-2000, because they were not always unique on the linkage variables (approx. 6%) or they immigrated to the Netherlands (<1%) in this period. As previous admissions of these subjects could be missed, this might have led to a slight overestimation of the incidence. A last aspect of our study that needs to be considered is the exclusion of non-uniquely linked hospital admissions and deaths. If such exclusion is related to determinants of AMI risk, it might have affected the incidence estimates to some extent. A pilot study¹⁴ suggested that non-uniqueness relates to large cities, foreign origin and age. The differences in these determinants between unique and non-unique persons were, however, relatively small.¹⁹ Moreover, substantial bias in the incidence estimates is likely prevented by excluding non-unique persons in the PR in the estimates of person-years at risk.

The incidence of AMI has been addressed in a number of studies.^{6-11,28,29} Yet, comparison between studies is difficult due to methodological differences (differences in data collection, registration methods, study population, case definition or research period). The different studies, however, were consistent with our finding of a higher incidence in men compared with women. In a Swedish national record linkage study, the incidence of first AMI (per 100,000) increased from 29 in men aged 25-44 years to 2322 in men aged 75-84 years and correspondingly in women from 8 to 1374. The male-to-female ratio decreased from 4.05 at age 45-54 years to 1.71 at age 75-84 years.³⁰ Our finding that a substantial proportion

of patients with a first AMI died out of hospital is in agreement with data from several other studies. Greenlee *et al.*³¹ reported that about 20% of first AMIs in a general population in the USA from 1992 to 1998 were detected only on death certificates. In another American study, the proportion of out-of-hospital deaths (both first and recurrent events) was estimated at 26% in 1996.³² In a study among the Jewish population of Jerusalem, 20% of men and 26% of women with a first AMI between 1995 and 1997 died out of hospital.²⁹ In a Scottish population-based record linkage study, 41% of the patients with a first AMI between 1986 and 1995 did not survive to be admitted to hospital.³² The risk of out-of-hospital death from a first AMI increased with age from 20% of all first AMI events (deaths plus hospital admissions) in persons <55 years to 62% in persons >85 years.³³ These estimates are comparable with those in our study. In the FINAMI study,³⁴ the proportion of out-of-hospital deaths of all coronary heart disease deaths was much higher and declined with age. From 1983 to 1997, the proportion of out-of-hospital deaths was 73% in men and 60% in women aged 35-64 years.³⁵ The proportion of out-of-hospital deaths ranged from 75% in men aged 35-54 years to 41% in men aged 85 years and over. Corresponding figures for women were 65 and 35%.

It seems that there has been no decline in the proportion of out-of-hospital deaths in the Netherlands, since Fracheboud has estimated that one third of patients with a suspected or confirmed AMI died out of hospital in 1985.³⁶

The large proportion of out-of-hospital deaths from a first AMI shown in our study reinforces the importance of improvements in primary prevention of AMI. Especially in patients who suddenly die before a medical doctor or an ambulance has arrived, treatment options are limited and mortality reduction can be achieved mainly by primary prevention. Furthermore, it is important to minimise the delay to initiation of treatment in patients with out-of-hospital cardiac arrest, as a shorter delay is shown to be associated with improved survival.³⁷

In conclusion, our study provides, for the first time, incidence estimates of first AMI based upon virtually the entire Dutch population. Expected differences in incidence with regard to age and gender were shown. The large proportion of out-of-hospital deaths reinforces the importance of primary prevention of AMI.

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