

# Extent of the Decrease of 28-Day Case Fatality of Hospitalized Patients With Acute Myocardial Infarction Over 22 Years

## Epidemiological Versus Clinical View: The MONICA/KORA Augsburg Infarction Registry

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**Background**—No data exist regarding time trends of 28-day case fatality (CF) of patients with presumed acute myocardial infarction (AMI) using epidemiological criteria, clinical criteria, and AMI classification after validation of presumed in-hospital AMI-related deaths (gold-standard criteria).

**Methods and Results**—From 1985 to 2004, we prospectively examined all 9210 AMI patients consecutively hospitalized in a large teaching hospital by using a broad epidemiological AMI definition (WHO-MONICA). Twenty-eight-day CF decreased significantly from 32% in 1985–1986 to 18% in 2003–2004, mostly because of a reduction in early deaths (<24 hours). When applying the clinical AMI definition, most of the early deaths were not counted as AMI related. A retrospective validation process from a sample of all early deceased patients by the epidemiological AMI definition (388/2076) and a prospective validation of the complete cohort in 2005–2006 revealed that only about 50% of early deaths are reclassified as a real fatal AMI using newer criteria resulting in a 28-day CF of 23% in 1985–1986 and 11% in 2005–2006. The difference between the AMI 28-day CF by applying gold-standard criteria and the clinical AMI 28-day CF (18% in 1985–1986 and 7% in 2005–2006) has decreased during recent years.

**Conclusions**—The application of broad epidemiological criteria for AMI overestimates 28-day CF by almost 2-fold compared with gold-standard criteria (after validation of early deaths) and almost 3-fold compared to the clinical definition. The growing similarity in 28-day CF between the clinically based definition and the gold-standard criteria implies that recent clinical-based registries may represent a realistic picture of trends regarding in-hospital AMI mortality. (*Circ Cardiovasc Qual Outcomes*. 2009;2:313-319.)

**Key Words:** myocardial infarction ■ epidemiology ■ prognosis

Although the crude categorization of deaths in noncardiovascular and cardiovascular disease (CVD) seems to be valid,<sup>1,2</sup> it is difficult to clearly differentiate whether CVD deaths are related to an acute myocardial infarction (AMI), with the classical pathophysiological mechanism of an occlusion or near occlusion of an epicardial coronary artery, or attributable to arrhythmogenic or nonarrhythmogenic death of a chronically diseased heart.<sup>3</sup> However, this uncertainty is not only related to the out-of-hospital setting, because early occurring in-hospital deaths often lack enough clinical data to clearly categorize them according to the clinical diagnosis of AMI.<sup>4</sup> As a consequence, in contrast to clinically based studies and registries, epidemiologically based studies usually use a broader definition of AMI, especially to avoid the

missing of out-of-hospital as well as early in-hospital AMI-related deaths (mostly referred to as coronary heart disease [CHD]-related deaths),<sup>5,6</sup> which otherwise would have been excluded by simply adopting clinical criteria. The latter based mainly on the detection of typical symptoms, certain ECG criteria, or rise of cardiac markers indicating myocardial injury. On the other hand, the adoption of these broader-based epidemiological AMI criteria lead to much higher rates of in-hospital case fatality (CF) of presumed AMI in comparison to using the clinical-based criteria.<sup>4</sup> This distinction may be of importance because the observation of a decrease in the death rate of AMI may depend on the definition and classification to be used (death classification artifact).<sup>7</sup> Additionally, the underlying cause of an observed decline may be attributable

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to different causes because decreases in death rates from chronic cardiovascular diseases may be predominantly attributable to improved primary and secondary prevention, whereas a decrease in death rates of real AMI may be more influenced by improved acute care.<sup>8</sup>

We therefore aimed to investigate time trends of in-hospital CF of AMI using broader based epidemiological criteria in conjunction with the classical clinical criteria, and AMI classification after the validation of presumed in-hospital AMI-related deaths.

### WHAT IS KNOWN

- For the out-of-hospital setting, it is difficult to clearly differentiate whether cardiovascular disease deaths are related to a real acute myocardial infarction, and it has been shown that CHD-associated deaths overestimated sudden cardiac deaths by 47%.

### WHAT THE STUDY ADDS

- Difficulty of correct classification of cardiovascular disease-related deaths is also seen for early occurring in-hospital deaths, where a high proportion—with conventional clinical definitions—are usually not considered as acute myocardial infarction cases, although they are in fact attributable to an acute manifestation of coronary heart disease.
- On the other hand, the application of broad epidemiological acute myocardial infarction criteria significantly overestimates fatal in-hospital short-term outcome compared to gold-standard criteria or clinical definition.
- During recent years, mortality rates between the clinical definition and the gold-standard criteria decreased, mainly because of a decrease of early occurring fatal cases implying effectiveness of improved care (acute as well as primary and secondary preventive).
- In addition, the latter observation implies that, for the future, clinical-based registries (or good validated hospital-based diagnosis) may be able to portray a realistic picture of trends in in-hospital acute myocardial infarction mortality.

### Methods

The population-based Augsburg Coronary Event Registry was implemented in October 1984 as part of the WHO MONICA (Monitoring trends and determinants on cardiovascular diseases) project.<sup>9</sup> Since 1996, the registry has worked within the framework of KORA (Cooperative Health Research in the Region of Augsburg). All cases of fatal coronary events and nonfatal AMIs of the 25- to 74-year-old inhabitants in the city of Augsburg and the 2 adjacent counties (about 400 000 inhabitants) are continuously registered. Methods of case finding, diagnostic classification of events, and data quality control have been described elsewhere.<sup>4,9,10</sup> Until December 31, 2000, diagnostic criteria for a nonfatal AMI were based on the WHO-MONICA-criteria.<sup>4,9,10</sup> Since January 1, 2001, all patients with AMI diagnosed according to European Society of Cardiology and American College of Cardiology criteria including troponin were also registered.<sup>11</sup> During the whole study period, measurement of all

enzymes indicating myocardial injury (creatinine-kinase, creatinine-kinase-MB, and, since 2001, troponin) was routinely performed. This report focuses on all patients with a suspected diagnosis of AMI who were hospitalized in the study region's major clinic (Klinikum Augsburg, an academic teaching hospital of the University of Munich and tertiary referral center offering angiography and percutaneous coronary intervention as well as heart surgery facilities) in which approximately 85% of all AMI cases of the study region are treated. All incident as well as recurrent cases were included. Patients transferred from other hospitals in which they had initially been treated for AMI were excluded. We used an intensive approach for ascertainment and identification of consecutive patients who were then evaluated according to rigorous validation criteria.

Using a list of specific admission diagnoses, the admission book of the clinic is screened for patients with suspected AMI or ischemic events on a daily basis. Subsequently, ward physicians are questioned via telephone to determine whether there is clinical evidence of AMI in patients meeting the screening diagnosis. The methods of classification of in-hospital occurring AMI cases were the same as for those being hospitalized via the emergency department by regularly screening the admission books of the intensive care wards and contacting the general ward physicians on a regular basis. The final criterion for inclusion in the register is a discharge diagnosis of AMI or of myocardial ischemia fulfilling the above-mentioned criteria. Treatment data are gathered in a concluding chart review. Data of fatal in-hospital events occurring within 24 hours after symptom onset were gathered as was the data acquisition for out of hospital deaths.<sup>9</sup> Only cases dying in the emergency department but not patients dead on arrival were counted as in-hospital fatal events. Briefly, the death certificates of all deceased within the study region were screened for a diagnosis suspicious for an AMI. Of those, the 3 regional health departments sent standardized questionnaires 2 to 4 weeks after the date of death to the last attending physician or coroner who return the information to the register (response rate >90%). The coroner and the last treating physician are asked to provide information on the events leading to death and the cardiovascular history of the deceased, including medication before death. Both information contained within the questionnaire and on the death certificate were used to classify the cases according to the international MONICA classification rules (diagnostic categories [DC]).

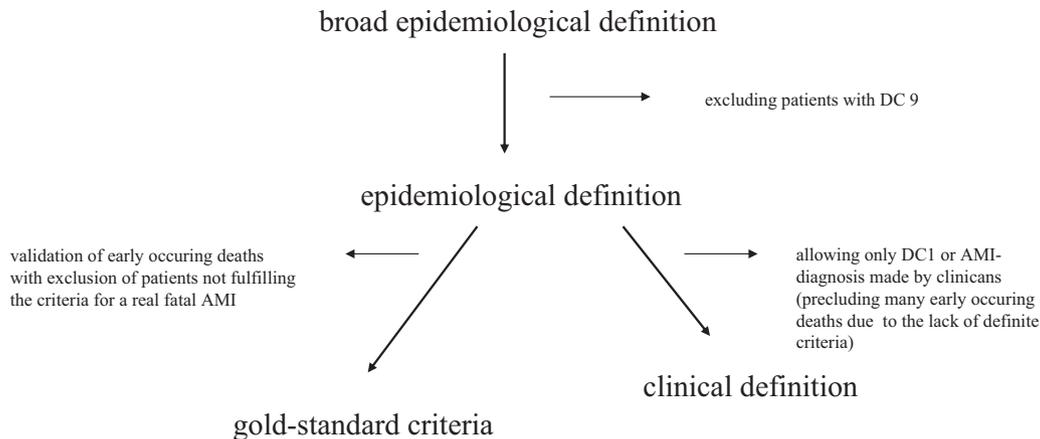
### Definition of AMI

#### "Broad" Epidemiological Definition

Including DC 1 (definite acute myocardial infarction, which requires definite ECG; or symptoms typical, atypical, or inadequately described, together with probable ECG and abnormal enzymes, or typical symptoms with abnormal enzymes independently from ECG coding, or fatal cases with naked-eye appearance of fresh myocardial infarction and/or recent coronary occlusion found at necropsy), DC 2 (possible acute myocardial infarction or coronary death); living patients: in cases with typical symptoms whose ECG and enzyme results do not place them in DC 1 and in whom there is not good evidence for another diagnosis for the attack, or fatal cases (not in DC 1) where there is no good evidence for another cause of death, clinically or at autopsy with symptoms typical or atypical or inadequately described, or without typical or atypical or inadequately described symptoms but with evidence of chronic coronary occlusion or stenosis or old myocardial scarring at necropsy (done in <5% of fatal cases) or with a good history of chronic ischemic heart disease such as definite or possible myocardial infarction, or coronary insufficiency or angina pectoris in the absence of significant valvular disease or cardiomyopathy), and DC 9 (fatal cases with insufficient data; cases with no autopsy, no history of typical or atypical or inadequately described symptoms, no previous history of chronic ischemic heart disease, and no other diagnosis).

#### Epidemiological Definition

DC 1+DC 2 excluding DC 9.



**Figure 1.** Illustration of AMI definitions. DC 9 includes fatal cases with insufficient data, including cases with no autopsy, no history of typical or atypical or inadequately described symptoms, no previous history of chronic ischemic heart disease, and no other diagnosis. Clinical definition includes DC 1, which means definite AMI and requires definite ECG; symptoms typical, atypical, or inadequately described, together with probable ECG and abnormal enzymes; typical symptoms with abnormal enzymes independently from ECG coding; fatal cases with naked-eye appearance of fresh myocardial infarction or recent coronary occlusion found at necropsy; or—without obligate ECG abnormalities as described in the MONICA manual—when a diagnosis of AMI was made by clinicians.

### Clinical Definition

All cases with DC 1 or—without obligate ECG abnormalities as described in the MONICA Manual—when a diagnosis of AMI was made by clinicians. The latter takes into account that, despite the missing of strict ECG abnormalities demanded by the MONICA-Manual, the diagnosis of AMI was made by a clinician recognizing all available clinical criteria.

### Gold-Standard Criteria (After Validation of the Epidemiological Definition)

In this regard it is important to mention that, according to the MONICA rules, simply the history of chronic ischemic heart disease (see above) attributed a fatal case as a CHD death according to the epidemiological definitions. Thus, from all the patients with a broad epidemiological definition of CHD death (DC 1, 2, and 9) who died during the first 24 hours from presumed beginning of symptoms ( $n=2076$ ) we took a 19% random sample ( $n=391$ ) for an intensified validation process. The sample was stratified according to year of death over the entire study period. The medical records of these patients were validated with regard to the cause of death through an intensive process of review and adjudication. All information obtained from the medical records was used, ie, ECG recordings, laboratory data, recordings about the presence of typical symptoms, previous nonischemic or ischemic heart disease, and the use of all prehospital as well as in-hospital therapy and diagnostic tools. For 3 patients the data quality was insufficient to allow any classification. A panel of 3 physicians reviewed each fatal case with disagreements being adjudicated by the committee chairman (B.K.). Cases were reclassified by using the criteria proposed by the Joint Committee of the European Society of Cardiology and American College of Cardiology, as well as other societies and research agencies to improve the consistency of case definitions in epidemiological and clinical studies.<sup>12</sup> Fatal events were classified into the following categories: “definite fatal AMI,” “probable fatal AMI,” or “possible fatal coronary event,” the latter 3 summarized as a “real fatal AMI,” as opposed to other causes of death which could be identified after this review process. Accordingly, the presence of an AMI by gold-standard criteria was assumed, when epidemiological AMI criteria were fulfilled excluding fatal cases not fulfilling the criteria for a real fatal AMI.

For a better understanding of the way of delineating the respective AMI definitions, we give an illustration in Figure 1.

The primary end point of the study was 28-day CF after having suffered a presumed AMI using different AMI definitions. Information about death of patients demitted earlier than 28 days from the

hospital was given, because death certificates of all patients dying in the study region are screened for having had a registered AMI.

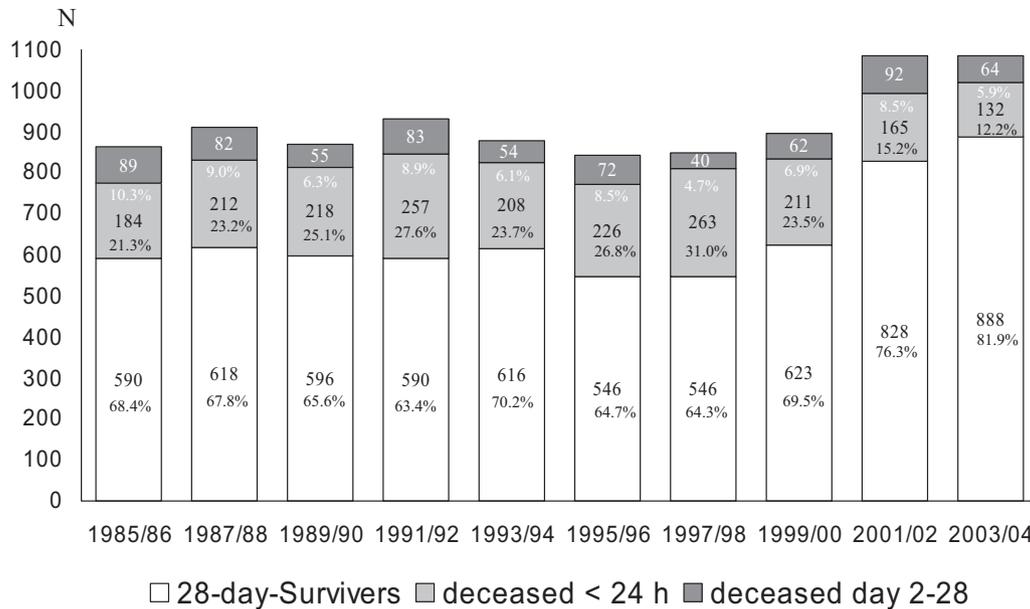
To investigate time trends in the number of patients who died during the first 24 hours, and the respective 28-day CF rates according to the AMI definitions used, we divided the study sample into eleven 2-year periods. For the investigation of time trends in the characteristics of the patients with validated “real fatal AMI” who died during the first 24 hours, because of the lower numbers, the study sample was divided into five 4-year time periods (1985 to 1988, 1989 to 1992, 1993 to 1996, 1997 to 2000, 2001 to 2004).

### Prospective Validation

Although more than 95% of hospital records were considered to be complete with good documentation and no significant change in the quality of the record over time was observed, the retrospective approach may be hampered by the necessity to gain all the information from the medical records. Thus we performed, in addition, a prospective study where all patients dying within 24 hours after hospitalization were screened regarding an underlying cardiovascular cause of death in addition to, and independently from, the screening process described above. Additional prompt (ie, mostly during the first 48 hours after death) standardized information was sought by a physician from the last treating physician or nurse in the ambulance, the emergency department, the coronary care unit, or on the general ward, as well as from family physicians, and coroners or medical examiners, next of kin, and other informants. In 60% of these cases an ECG from shortly before the occurrence of death was available, in 70% first laboratory results including creatinine-kinase and troponin, and in 90% information regarding the last hours before death were available from chart review and interviews of the last treating physician or next of kin. This prospective evaluation took place from August 2004 to August 2006 and, for convenience, the prospective data are summarized as the years 2005–2006, whereas the data regarding the retrospective approach of validation extended until July 2004.

### Statistical Analysis

The associations between time periods and 28-day CF were examined using logistic regression, while modeling time periods as an 11-level categorical variable giving the  $P$  for trend; probability values  $<0.05$  were considered as statistically significant. We decided not to present the data separately for men and women because the differences in CF estimations according to the respective AMI definitions did not differ between men and women.



**Figure 2.** Number of hospitalized patients with AMI classified by the broad epidemiological definition who survived 28 days, who died during the first 24 hours, and who died from day 2 to 28.

All analyses were carried out with the SAS System for Windows, release 8.2. The authors had full access to the data and take responsibility for its integrity. All authors have read and agree to the manuscript as written.

## Results

### Entire Population

From 1985 until the end of 2004, data from a total of 9210 patients hospitalized with a suspected diagnosis of AMI using the broad epidemiological definition (DC 1, 2, 9) were consecutively documented. Figure 2 shows the number of patients who died during the first 24 hours versus those who died between days 2 and 28 versus those surviving the first 28 days and the respective percentages over time.

While there was little change in the number of hospitalized fatal and nonfatal AMIs until the years 1999–2000, there was an increase after the year 2000. The latter was exclusively attributable to the increasing numbers of patients with non-fatal AMI. In contrast, there was a decrease of early occurring

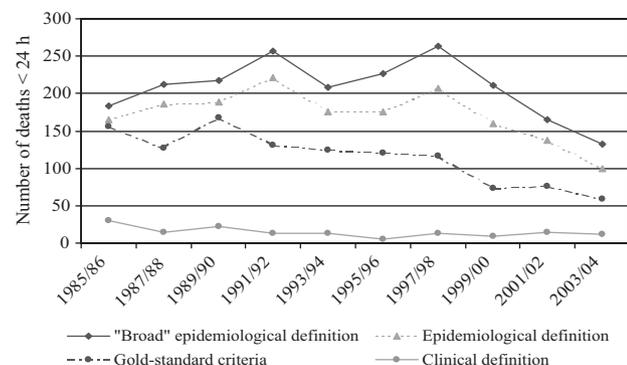
(<24 hours) deaths since the years 1999–2000. This is graphically illustrated in Figure 3.

When cases with insufficient data (DC 9) were excluded (epidemiological definition), there were 17% less early deaths with a similar trend in decline (Figure 3). On the other hand, by only including early deaths with a clinical diagnosis of AMI the numbers of early deceased patients were rather low with no significant change over time.

### Retrospective Validation Sample

Table 1 shows how all 388 early fatal AMI cases according to the broad epidemiological definition of our retrospective validation sample were classified by using the classification criteria proposed by the American Heart Association, World Heart Federation, and the European Society of Cardiology Councils on Epidemiology and Prevention.<sup>12</sup>

It shows that only 52% of these cases are attributable to a real fatal AMI. Eighteen percent had a longstanding history of ischemic cardiomyopathy without any signs of acute ische-



**Figure 3.** Number of in-hospital deaths occurring during the first 24 hours after beginning of symptoms according to AMI definition.

**Table 1. Classification of Early Occurring Deaths After Validation**

Death Occurring During the First 24 Hours After Hospitalization	n=388	
	n	%
Definite AMI*	141	36.3
Probable AMI*	23	5.9
Possible AMI*	39	10.1
No AMI, death attributable to ischemic but not acute ischemic cardiomyopathy	70	18.0
No AMI, death attributable to nonischemic cardiomyopathy	26	6.7
No AMI, definite other cause of death	57	14.7
Not classifiable attributable to missing data	32	8.3

\*Definite, probable, and possible AMI are summarized as a real fatal AMI.

**Table 2. Characteristics of the Early Deceased Patients With a Validated Diagnosis of Real Fatal AMI**

	1985 to 1988 (n=43)	1989 to 1992 (n=35)	1993 to 1996 (n=53)	1997 to 2000 (n=41)	2001 to 2004 (n=31)	P Value
General characteristics						
Men	36 (84%)	26 (74%)	35 (66%)	27 (66%)	27 (87%)	0.1
Age (mean±SD), y	64±9	65±9	65±9	65±9	63±9	0.86
Medical history						
Known EF <40%	8 (19%)	13 (37%)	13 (25%)	4 (10%)	5 (16%)	0.05
Myocardial infarction	29 (67%)	26 (74%)	29 (55%)	10 (24%)	16 (52%)	0.001
History of hypertension	25 (58%)	24 (69%)	34 (64%)	28 (68%)	21 (68%)	0.85
History of hyperlipidemia	17 (22%)	16 (46%)	21 (40%)	7 (17%)	16 (52%)	0.02
History of diabetes	9 (21%)	17 (49%)	18 (34%)	19 (46%)	12 (38%)	0.08
Circumstances						
Already hospitalized	17 (39%)	10 (29%)	15 (28%)	14 (34%)	12 (39%)	0.71
Prehospital reanimation*	5 (19%)	9 (36%)	16 (42%)	15 (56%)	15 (79%)	0.001
Prehospital shock*	9 (35%)	13 (52%)	26 (68%)	16 (59%)	16 (84%)	0.01

EF indicates ejection fraction.

\*Only patients hospitalized with emergency system (n=135).

mia, and in 6.7% a nonischemic cardiomyopathy was diagnosed. The latter 2 diagnoses were mainly patients already hospitalized with symptoms of a failing heart. Looking at time trends in the classification of presumed AMI-related deaths revealed that over time there was a trend for classification of fewer patients as a real fatal AMI. The respective proportions of early deceased patients allocated to be attributable to a real AMI were 73%, 47%, 61%, 57%, 60%, 51%, 42%, 33%, 42% ( $P<0.001$ ), and 40%, respectively, for the time periods 1985–1986 until 2003–2004.

The number of deaths when only the proportion of validated real fatal AMI evaluated in the validation sample were counted for the whole number of epidemiologically defined AMI-related early in-hospital deaths are given in Figure 3. Characteristics of patients with validated real fatal AMI over time are given in Table 2.

**Prospective Validation**

From August 2004 to August 2006 prospective identification and validation of all patients with an epidemiologically defined early AMI-related death by MONICA/KORA protocol was done in a similar way to the retrospective approach. It revealed that, similarly to the results of validation in the last years of the retrospective approach, 47% of epidemiologically defined AMI-related deaths were attributable to a real fatal AMI (45 of 95 deaths).

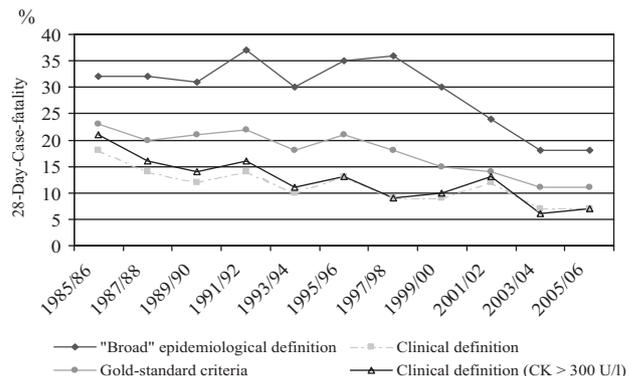
**Effect of AMI Definition on the Calculation of 28-Day CF**

Figure 4 shows the respective 28-day CF according to the AMI-definition used. The 28-day CF is also shown when only the proportion of the really fatal AMI cases in addition to the deaths occurring from days 2 to 28 are counted. Application of this gold-standard AMI criteria resulted in a 28-day CF lying between that when using the broad epidemiological definition and that with the clinical definition. However, since 2001, the difference in 28-day CF rates between the clinical definition and the gold-standard criteria decreased. A

more conservative clinical definition including only AMIs with a significant rise in creatinine-kinase (>300 U/L) showed the same trend (Figure 4). Adjustment for a history of previous AMI did not change the trend for all definitions used, and there were no statistical significant differences (testing for interaction by sex and time,  $P>0.05$ ) in the respective 28-day CF between men (decrease from 31%, 17%, and 23% in 1985–1986 to 18%, 7%, and 11% in 2005–2006 using the broad epidemiological definition, the clinical definition, and the gold-standard criteria, respectively) and women (decrease from 32%, 19%, and 23% in 1985–1986 to 19%, 8%, and 11% in 2005–2006, respectively).

**Discussion**

The estimation of in-hospital short-term mortality mainly depends on the definition of AMI and the classification of early in-hospital cardiac deaths. Our data show that using a broader epidemiological-based definition results in much



**Figure 4.** Twenty-eight-day CF according to AMI definition ( $P$  for trend in the decline of 28-day CF  $<0.001$  for all definitions; adjusting for age, history of hypertension, history of hyperlipidemia, history of previous myocardial infarction, and history of diabetes in analyzing the trend in 28-day CF by the broad epidemiological and the clinical definitions did not change the  $P$  for trend).

higher CF rates when compared to using a clinical-based definition. A crucial point in this regard is the classification of early occurring deaths (<24 hours after hospitalization or beginning of symptoms). A detailed validation of these cases revealed that only around 50% of early in-hospital deaths originally attributed to be attributable to an AMI, by applying the epidemiological approach, are attributable to a real fatal AMI. This is an important finding because the formerly proposed rule of thumb that two thirds of fatal AMI cases die out of hospital, and again more than two thirds of all deaths after hospitalization occur during the first 24 hours,<sup>4,5</sup> is unlikely to be true because, at least for the in-hospital setting, we could show that a significant number of presumed AMI-related deaths are actually not attributable to an AMI, but are rather the result of either longer existing heart disease in a final stage or other causes. A previous study which, however, did not implement such an extensive identification process of all in-hospital occurring deaths, revealed during an observation period of 1 year (1992) that 30-day fatality varied between 14% and 23% depending on different AMI definitions and classification systems used.<sup>13</sup> Another study in the out-of-hospital setting looking for the validity of classification of CHD-related sudden death similarly revealed that out-of-hospital CHD-associated deaths overestimated sudden cardiac deaths by 47%.<sup>14</sup>

On the other hand, regardless of the AMI definition and classification used, there was a sharp decline in 28-day CF among hospitalized patients with presumed AMI over a period of 22 years. This decline is attributable to several mechanisms. First, there is a decrease in the absolute number of early occurring in-hospital deaths when using the epidemiological definitions before as well as after validation of early fatal cases. Second, there is an increase in the crude number of surviving patients which therefore influences the denominator and may mainly be attributable to the introduction of troponin measurement allowing the detection of more, and presumably, milder AMI cases with a better short-term prognosis.<sup>15,16</sup> However, using a more conservative clinical definition including only AMIs with a significant rise in creatinine-kinase (>300 U/L) showed the same trend (Figure 4). Therefore, although the incidence of nonfatal AMIs is increased with the additional implementation of troponin the positive trend in 28-day CF is independent of this new classification because considering only “creatinine-kinase-positive” cases with the clinical definition showed the same trend. Accordingly, from these data, it could be inferred that there must be 2 mechanisms responsible for the observed decline. First, the sharp decline of the crude number of fatal cases during the first 24 hours, which is at least in 50% attributable to nonacute AMI cases, may be attributable to a decreasing incidence of severe cases of mostly ischemic and nonischemic cardiomyopathies and, therefore, may be an indication of improved primary and secondary prevention in our population.<sup>17</sup> This is in accordance with the observation of the decreasing incidence of prehospital presumably CHD-related fatal cases.<sup>17</sup> Secondly, the decline of early occurring fatal cases as well as 28-day CF by applying gold-standard as well as clinical AMI criteria may also imply improved acute care. In fact, an earlier analysis of our AMI population has

shown that the use of evidence-based therapies increased substantially over the study period.<sup>18</sup> In the latter, however, we had no information about the very early deceased patients. The analysis of our sample of validated early AMI-related deaths revealed that the proportion of very-high-risk patients (ie, those with prehospital resuscitation or cardiogenic shock) increased over time, suggesting that only those remained where no more meaningful therapeutic option was available.

Of interest, because of these mechanisms, the observed difference in the estimation of 28-day CF when using the clinically based definition and the gold-standard criteria decreased in recent years, implying that the real fatal AMI-related deaths missed by using only the clinical definition are negligible. Therefore, for the future, clinical-based registries may be able to give a realistic picture of trends in in-hospital AMI mortality.<sup>19</sup>

### Limitations

The introduction of more sensitive markers of myocardial infarction might have influenced the outcomes, and as outlined above, this has led to the detection of more nonfatal events classified as AMI. However, although one could speculate that using a more sensitive marker must also lead to the detection of more fatal cases classified as AMI-related, the crude number of deaths estimated with the broad epidemiological definition has decreased markedly over recent years. In addition, it has to be mentioned that monitoring trends in in-hospital AMI mortality does not describe the trends in mortality in the community, because of biases relating to which patients reach hospital and estimates of trends based on data for only those that reach hospital will give a biased view of overall CHD/AMI mortality trends and burden. Because of restrictions to the original MONICA protocol, patients  $\geq 75$  years were not registered, precluding assumptions of interaction between older age and temporal change in mortality.

### Conclusions

The estimation of in-hospital short-term mortality is mainly dependent on the definition of AMI used and the classification of early in-hospital cardiac deaths. The application of broad epidemiological AMI criteria overestimates fatal in-hospital short-term outcome almost 2-fold when compared to gold-standard criteria (after validation of early deaths) and almost 3-fold compared to a clinical definition. However, independently from the definition used, a sharp decline of 28-day CF was observed over the past 22 years. The observed difference in the estimation of 28-day CF between the clinically based definition and the gold-standard criteria decreased during the last years implying that, for the future, clinical-based registries may be able to portray a realistic picture of trends in in-hospital AMI mortality.

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## Disclosures

None.

## References

- Goldberg RJ, Glatfelter K, Burbank-Schmidt E, Lessard D, Gore JM. Trends in community mortality due to coronary heart disease. *Am Heart J*. 2006;151:501–507.
- Goraya TY, Jacobsen SJ, Belau PG, Weston SA, Kottke TE, Roger VL. Validation of death certificate diagnosis of out-of-hospital coronary heart disease deaths in Olmsted County, Minnesota. *Mayo Clin Proc*. 2000;75:681–687.
- Simon SR, Powell LH, Bartzokis TC, Hoch DH. A new system for classification of cardiac death as arrhythmic, ischemic, or due to myocardial pump failure. *Am J Cardiol*. 1995;76:896–898.
- Kuch B, Bolte HD, Hörmann A, Meisinger C, Löwel H. What is the real hospital mortality from acute myocardial infarction? Epidemiological vs clinical view. *Eur Heart J*. 2002;23:714–720.
- Rosamond WD, Chambless LE, Folsom AR, Cooper LS, Conwill DE, Clegg L, Wang CH, Heiss G. Trends in the incidence of myocardial infarction and in mortality due to coronary heart disease, 1987 to 1994. *N Engl J Med*. 1998;339:861–867.
- Tunstall-Pedoe H, Kuulasmaa K, Mähönen M, Tolonen H, Ruokokoski E, Amouyel P. Contribution of trends in survival and coronary-event rates to changes in coronary heart disease mortality: 10-year results from 37 WHO MONICA project populations. Monitoring trends and determinants in cardiovascular disease. *Lancet*. 1999;353:1547–1557.
- Luepker RV. Decline in incident coronary heart disease: why are the rates falling? *Circulation*. 2008;117:592–593.
- Ford ES, Ajani UA, Croft JB, Critchley JA, Labarthe DR, Kottke TE, Giles WH, Capewell S. Explaining the decrease in U.S. deaths from coronary disease, 1980–2000. *N Engl J Med*. 2007;356:2388–2398.
- Löwel H, Lewis M, Hörmann A, Keil U. Case finding, data quality aspects and comparability of myocardial infarction registers: Results of a South German register study. *J Clin Epidemiol*. 1991;44:249–260.
- The World Health Organization MONICA Project (monitoring trends and determinants in cardiovascular disease): a major international collaboration. WHO MONICA Project Principal Investigators. *J Clin Epidemiol*. 1988;41:105–114.
- Alpert JS, Thygesen K, Antman E, Bassand JP. Myocardial infarction redefined- a consensus document of The Joint European Society of Cardiology/American College of Cardiology Committee for the redefinition of myocardial infarction. *J Am Coll Cardiol*. 2000;36:959–969.
- Luepker RV, Apple FS, Christenson RH, Crow RS, Fortmann SP, Goff D, Goldberg RJ, Hand MM, Jaffe AS, Julian DG, Levy D, Manolio T, Mendis S, Mensah G, Pajak A, Prineas RJ, Reddy KS, Roger VL, Rosamond WD, Shahar E, Sharrett AR, Sorlie P, Tunstall-Pedoe H; AHA Council on Epidemiology and Prevention; AHA Statistics Committee; World Heart Federation Council on Epidemiology and Prevention; European Society of Cardiology Working Group on Epidemiology and Prevention; Centers for Disease Control and Prevention; National Heart, Lung, and Blood Institute. Case definitions for acute coronary heart disease in epidemiology and clinical research studies: a statement from the AHA Council on Epidemiology and Prevention; AHA Statistics Committee; World Heart Federation Council on Epidemiology and Prevention; the European Society of Cardiology Working Group on Epidemiology and Prevention; Centers for Disease Control and Prevention; and the National Heart, Lung, and Blood Institute. *Circulation*. 2003;108:2543–2549.
- Packham C, Gray D, Weston C, Large A, Silcocks P, Hampton J. Changing the diagnostic criteria for myocardial infarction in patients with a suspected heart attack affects the measurement of 30 day mortality but not long term survival. *Heart*. 2002;88:337–342.
- Fox CS, Evans JC, Larson MG, Lloyd-Jones DM, O'Donnell CJ, Sorlie PD, Manolio TA, Kannel WB, Levy D. A comparison of death certificate out-of-hospital coronary heart disease death with physician-adjudicated sudden cardiac death. *Am J Cardiol*. 2005;95:856–859.
- Roger VL, Killian JM, Weston SA, Jaffe AS, Kors J, Santrach PJ, Tunstall-Pedoe H, Jacobsen SJ. Redefinition of myocardial infarction: prospective evaluation in the community *Circulation*. 2006;114:790–797.
- Amit G, Gilutz H, Cafri C, Wolak A, Ilia R, Zahger D. What have the new definition of acute myocardial infarction and the introduction of troponin measurement done to the coronary care unit? Impacts on admission rate, length of stay, case mix and mortality. *Cardiology*. 2004;102:171–176.
- Löwel H, Meisinger C, Heier M, Hörmann A, von Scheidt W. Myocardial infarction and coronary mortality in Southern Germany. *Dtsch Arztebl*. 2006;103:A616–622.
- Kuch B, Heier M, von Scheidt W, Kling B, Hoermann A, Meisinger C. 20-year trends in clinical characteristics, therapy and short-term prognosis in acute myocardial infarction according to presenting electrocardiogram: the MONICA / KORA AMI Registry (1985–2004). *J Intern Med*. 2008;264:254–264.
- Zeymer U, Senges J. Why do we need prospective registries in patients with acute myocardial infarction? *Eur Heart J*. 2003;24:1611–1612.

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